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CENTRIFUGATION OF THE NERVOUS SYSTEM—A METHOD FOR NEUROCYTOLOGIC STUDY

AN EXPERIMENTAL INVESTIGATION OF CELLULAR CHANGES IN COMMOTION

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THE PROBLEM OF COMMOTION

In spite of diligent research and much discussion, the problem of commotion still contains many mysteries. Various theories have been developed as to the effect of traumatism to the skull. Some authors have paid especial attention to vascular changes, and have held that vasomotor disturbances or hemorrhages in the brain substance are responsible for the symptoms of commotion. Others contend that sudden and violent displacements of the cerebrospinal fluid could, according to hydrodynamic principles, produce the nervous disturbances. Finally, a few authors have postulated cellular changes brought about by the trauma.

In cases of hemorrhage and laceration of nervous tissue, there is no difficulty in understanding the clinical sequences of the traumatism, but hydrodynamic waves of the cerebrospinal fluid and cellular changes were purely hypothetic. Cellular changes after commotion have only been demonstrated as more or less extensive, late degeneration. Anatomic examination during the acute stage of commotion has never given clear evidence of the nature of these cellular alterations. Undoubtedly, the complete absence of such evidence is the reason why the majority of writers maintain that the degenerations found some time after the traumatism are secondary to vascular changes. There are not a few authors who emphatically deny the existence of real primary cellular alterations in commotion; and many regard commotional syndromes as purely functional and devoid of anatomic alterations.

The difficulty of the problem is evident from the discussion of traumatic neurosis or railway-spine which has waged since the eighties, especially in Germany. Oppenheim stoutly defended the opinion that, in commotion, fine cellular alterations were the cause of many of the

clinical symptoms. Charcot and his German adherents maintained that the commotional symptoms were all functional or hysterical. This question divided German neurologists into two camps, and the discussion was one of the most vivid on a neurologic problem of modern times.

It was only natural that the question should again arise during the war, with its innumerable cases of cerebral and spinal commotion. In particular, the syndromes exhibited by people who had been subjected, at close range, to detonations of high explosives without having been hit directly (shell-shock), aroused widespread interest. In Germany, the veteran Oppenheim [1] held to his old concept, in spite of the fact that he had against him the majority of German neurologists. In France, England and America, the discussion was also keen. At the beginning of the war, there was undoubtedly a tendency to consider shell-shock without visible signs of injury purely functional, that is, "sine materia." But an increasing number of authors, especially toward the end of hostilities, have discouraged this concept as too one-sided. Certain symptoms in the commotional syndromes may be emotional, but others cannot be explained as purely functional. These must then be related to alterations of the nervous system brought about by the traumatism. Unfortunately, the efforts of the war period did not solve the problem. Perhaps there is at present a greater tendency to look for organic causes in the syndrome of commotion than before the war; but still, the question as to where the emotional factor begins and the organic factor ends, belongs to the most difficult diagnostic problems in present-day neurology.

Recent discussion has not been able to solve the question of the nature of the effect produced by physical violence on the nervous system. Lacerations of the nervous substance due to contrecoup and rupture of coarser vessels with consequent hemorrhages are often seen at necropsies. These lesions are left out of consideration in the following discussion. Many cases, with intense commotional symptoms from various regions of the nervous system, are reported in the literature, in which no manifest anatomic lesion could be demonstrated. In such cases several investigators have postulated the existence of the so-called molecular or microstructural alterations brought about by the concussion. Among these authors are to be found representatives of several nations including Roussy and Lhermitte,[2] Carver and Dinsley, [3]

1. Oppenheim: Die Neurosen in Folge von Kriegsverletzungen, Berlin: 1916.

2. Roussy, Gustave, and Lhermitte, Jean: Les blessures de la moelle et de la queue de cheval, Paris: Masson et Cie, 1918; Psychoneuroses de guerre, ibid., 1917.

3. Carver, Alfred, and Dinsley, A.: Some Biological Effects Due to High Explosives, Brain **42**:113 (June) 1919.

von Sarbo,[4] Bauer,[5] Henneberg, Harris, Duret[6] and a considerable number of others.

The term "molecular lesions" of the nerve cells originated with Erichsen in 1875. He thought that as a magnet is weakened by violent concussion, supposedly by an alteration of the mutual relations between the molecules, so the elements of the cells might be interefered with, in a similar way, in commotion. This idea was further developed by Obersteiner.[7]

Schmauss[8] must be given credit for the first exact experiments on cellular changes in commotion. He tied animals to a board and struck repeated heavy blows on the board. Afterward he was able to show widespread degenerations in the nervous system (tigrolysis of the cells and changes in the axis cylinders and their myelin sheaths). Among investigators who have continued this experimental work may be mentioned Bikeles, Luzenberger,[9] Kirchgasser,[10] Jakob,[11] Tscherbak and lately Cornil.[12] The usual method has been to inflict different kinds of trauma on animals. These authors have studied chiefly the changes that exist some time after the traumatism. They have then been able to show degenerative processes affecting cells, nerve fibers and glia.

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4. Von Sarbo, A.: Ueber den sogenannten Nervenchok nach Granat und Schrapnell-Explosionen, Wien. klin. Wchnschr. **28**: Pt. 4, 1915; Ueber die durch Granat- und Schrapnell-Explosionen entstandenen Zustandsbilder, ibid. **29**: Pt. 20, 1916; Die durch Granatfernwirkung entstandene Taubstummheit eine medulläre Erkrankung, Med. Klin. **12**: Pt. 38, 1916; Granatfernwirkungsfolgen und Kriegshysterie, Neurol. Zentralbl. **36**: Pt. 9, 1917.

5. Bauer: Ueber Rückenmarkserschütterung, Wien. med. Wchnschr. **67**: 2052, 1917.

6. Duret, H.: Commotions graves mortelles, sans lésions, et lésions générales étendues sans commotion dans les traumatismes cérébraux, Rev. neurol. **36**:888, 1920; Discussion générale sur les accidents nerveux déterminés par la déflagration de fortes charges d'explosifs, Société de Neurologie, April 6-7, 1916; Rev. neurol. **32**:575, 1916.

7. Obersteiner: Ueber Erschütterung des Rückenmarks, Wien. med. Jahrb. **3** and **4**:531, 1879.

8. Schmauss: "Commotio Spinalis," Ergeb. d. allg. Pathol. u. pathol. Anat. p. 594, 1897; Beiträge zur pathologischen Anatomie der Rückenmarkserschütterung, Virchow's Arch. **122**:326, 1890.

9. Luzenberger: Anatomie pathologique du traumatisme nerveux, Arch. d. neurol., 1897.

10. Kirchgasser: Experimentelle Untersuchungen über Rückenmarkserschütterung, Deutsch. Zeitschr. f. Nervenheilk. **11**:406, 1897, and **13**:422, 1898.

11. Jakob: Experimentelle Untersuchungen über die traumatischen Schädigungen des Zentralnervensystems, Histolog. u. histopathol. Arb. über Grosshirnrinde **5**:182, 1912.

12. Cornil, Lucien: Commotion médullaire directe, Paris: Librairie le François, 1921.

Concerning the histologic findings in the acute stage of commotion, the statements are not so unanimous. They are mostly minute hemorrhages or congestion of the nervous tissue. Jakob gives a detailed description of the acute stage. He finds in medullary commotion a granular homogenization both of the cytoplasm and the karyoplasm of the nerve cells. Further, he has observed eccentric location of the nucleus. Todde has found rupture of the endocellular fibrillary net, or a homogenization of these fibrils.

Summing up these investigations, there are many evidences of degenerative processes some time after the trauma, but, in the acute stage, the histologic findings are few when rupture and disturbance of the vessels are excluded.

In spite of the experimental evidence, the cellular lesions are not clearly defined in the literature. Chavigny [13] declared, in 1918, that no precise documentation of the cellular changes in commotion existed, and that all experiments had failed to elucidate the problem. Some authors [14] decline entirely to accept the existence of such lesions. Von Sarbo denotes the cellular alterations in commotion by the term microstructural and means by this: squeezings of the nervous substance, microhemorrhages and changes in the meninges brought about by the physical concussion of the cells and fibers. Roussy and Lhermitte admit the possibility of such fine fibrillar and cellular lesions, but state that it is at present impossible to say anything definite about the anatomic or dynamic nature of these lesions.

From the fact that colloidal suspensions change their physical properties on being exposed to shaking, Marinesco [15] concludes that the concussion acts on the proteolytic ferments of the cell, thereby changing the physical nature of the colloids in the cells and fibers. Gordon Holmes [16] writes on spinal concussion: "The most probable explanation is that put forward by Fickler,[17] according to which the cord is made to oscillate within the spinal canal by the impact on the vertebral spinal column, and, as its movements will obviously not be synchronous with

13. Chavigny, P.: Les explosions du champ de bataille, Paris méd. **8**:341, 1918.

14. Kocher: Die Verletzungen der Wirbelsäule, zugleich ein Beitrag zur Physiologie des menschlichen Rückenmarks, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **1**:415, 1896.

15. Marinesco, G.: Lésions commotionelles expérimentales, Rev. neurol. **34**: 329, 1918.

16. Holmes, Gordon: On Spinal Injuries of Warfare, Goulstonian lectures, British M. J., 1915.

17. Fickler: Experimentelle Untersuchungen zur Anatomie der traumatischen Degeneration und der Regeneration des Rückenmarkes, Deutsch. Zeitschr. f. Nervenheilk. **29**:1, 1905.

those of the column, it may be directly bruised against the walls of the canal, while at the same time the sudden jarring of the cord produces a physical disturbance in its tissues and especially in the fluid axoplasm of its fibres."

In the literature on commotion, there is a strong tendency to emphasize vasomotor changes as the main cause of the commotional symptoms in the acute stage (Ricker, Bonnet [18] and others). Very often at the necropsies in cases in which death occurred during the acute stage of the commotion, the only anatomic finding is a great number of microscopic bleedings scattered over large parts of the nervous system (Huet, Kocher,[14] Hoven,[19] Lépine,[20] Mott and others). Such bleedings are supposed to cause laceration of the tissues, cells and fibers, with consecutive stasis phenomena from both lymphatic and blood vessels. These secondary effects are sometimes held responsible for the degenerative process which is the most common anatomic consequence of the commotion.[21] The mechanism of spinal commotion in particular is explained in this way. Many authors regard such vascular changes as the most essential anatomic feature of the lesion (Marburg,[22] Licen, Jakob,[11] Marie and Chatelin). So-called "retarded" commotional symptoms also find their explanation in this way according to Léri.[23]

In order to analyze the effect of trauma in bringing about commotion of the nervous system, we have to consider the nature of the forces acting on the body when the commotion is established. Commotion is produced by blows against the skull or in the spinal region. Such a blow must mean a concussion of the parts that are hit, as the blow will transmit its energy to the body exposed to it. In principle, the same effect will be produced by a blow from a heavy object as by the intense atmospheric disturbances that follow an explosion ("vent de l'obus").

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18. Bonnet, M.: Contribution à l'étude des effets des explosions de guerre sur l'organisme, Thèse de Nancy, 1918.

19. Hoven, H.: Les commotions des centres nerveux par éclatement des projectiles à proximité immédiate, Arch. méd. Belges, **71**: (June) 1918.

20. Lépine, Jean: Commotion des centres nerveux par explosion, Acad. de médécine, Paris, July 4, 1916.

21. De Lisi, L.: Recherches expérimentales sur les altérations nerveuses centrales chez les animaux soumis à la commotion cérébrale, Riv. sper. di Freniat. **61**: Pt. 2, 1915.

22. Marburg, Otto: Zur Frage der Beurteilung traumatischer Neuronen im Kriege, Wien. klin. Wchnschr. **29**:281, 1916; Zur Pathologie der Kreigsbeschädigungen des Rückenmarks, Arbeiten aus dem Neurol. Inst. (Obersteiner), Wien, 1919.

23. Léri, André: Les commotions "retardées" par l'explosion d'obus, Presse méd. **26**:403 (Aug. 5) 1918; Commotions et émotions de guerre, Paris: Masson et Cie, 1918.

In the latter case the individual is caught by the intense wave of atmospheric compression that follows the detonation and is violently thrown a shorter or longer distance to the ground. Reports from the war mention that the victims of commotion were often found buried in the ground.

It must be assumed a priori that the different cellular constituents of the nervous system have different specific gravities. They must accordingly react with different velocities to external physical forces. It must then be expected that physical forces imposed on the neuraxis cause displacement, not only of the external interrelations of cells, but also of the relations between the intracellular constituents.

Tillman [24] attacked the problem experimentally from this point of view and paid special attention to the differences in specific gravity of various constituents of the brain substance. According to this author, the white substance and the blood, as specifically heavier substances, have a greater inertia than the gray matter. Accordingly, if there is imposed a sudden movement on the brain as a whole, there will be established a disturbance of the mutual relations of these substances, which may lead to lacerations at the junction between white and gray matter and to rupture of minute vessels.

The forces in concussion act in opposite directions; compression waves are followed by decompression waves. Even if displacement of the cellular constituents takes place during the actual concussion, the effect may be neutralized by the displacement in the opposite direction that is likely to follow. Histologic signs of displacement, therefore, need not be found after the concussion. In fact, no conclusive signs of the postulated displacements have ever been demonstrated, either in the clinical or the experimental records.

But it is logical to conceive that displacement of the intracellular parts may nevertheless lead to loss of function of the cells. The clinical facts indicate very strongly that there is a widespread paralysis of function in the acute stage of commotion. In cases in which death occurred in the acute stage of the commotion and the most careful histologic examination failed to reveal anatomic changes, such cellular alterations have been held responsible for the fatal issue by several authors.

To study the effect of physical forces acting indirectly on the contents of the spinal and cranial cavities, the writer has exposed parts of the nervous system from different animals (crab, frog, mouse and rabbit) to centrifugation. To complete the series, pieces of the human

24. Tillman: Die Theorie der Gehirn- und Rückenmarkserschütterung. Arch. f. klin. Chir. **59**: 1899.

medulla oblongata were also treated in the same way. The forces acting in centrifugation have an advantage over those acting in concussion in that they work only in one direction. This advantage makes it possible by experiment to determine whether a physical force acting indirectly on the nerve cells can produce an effect within them. If centrifugal force produces displacements of the cellular constituents, the forces producing commotion must be assumed to have a similar effect and a similar impairment of function must result, even if the histologic effect in the two cases is different.

Further, centrifugation of nerve cells has proved to be a valuable method of studying various neurocytologic problems. The displacement brought about by centrifugation may be considered as a form of endocellular dissection.

Centrifugation of the nervous system has been carried out before by Arndt.[25] Pieces of cortex from the human brain, obtained twelve hours after death, were exposed by him to centrifugation for four hours, and then to further centrifugation in formaldehyd solution for two hours. He found only negligible changes. In several cells he found that the nucleus had been moved distad, without alteration in the shape of the nucleus itself. Arndt also centrifugated brains of frogs and found that the nucleolus in the cells was easily moved by the centrifugal force. He thinks that such displacements prove that the various cellular constituents have different specific gravities. But he concludes: "Die spezifischen Gewichtsunterschiede sind nur gering, andererseits muss die Befestigung von Zelle, Kern, Kernkörperchen in ihrer Umgebung von erstaunlicher Vollkommenheit sein." He does not draw from his experiments any conclusions in regard to the mechanism of commotion. Forel,[26] in 1919, performed centrifugation on animals and human beings in order to produce a slight commotional stage, which might serve as a substitute for narcosis. He did not combine his studies with histologic examinations of the nervous system.

HISTOLOGIC PROBLEMS

A study of the histologic literature of later years gives the impression that histologic methods, hitherto so much used, have in many respects reached the limit of their efficiency for elucidating morphologic cell problems. There is a conspicuous tendency among histologists to

25. Arndt, G.: Traumatische Erkrankungen des Rückenmarks (Commotio spinalis.), Ergebn. der allg. Pathol. **9**:1, 1903.

26. Forel, O. L.: Contribution à l'étude des traumatismes cérébraux, Schweiz. Arch. f. Neurol. u. Psych. **4**: 1919.

discredit the older histologic methods, for the reason that all fixation methods that make use of protein coagulating agents cause severe damage to the delicate cell constituents. The cell stained after fixation presents a picture, not only of a dead cell, but of one more or less severely deformed. To eliminate such artefacts, various investigators have begun to study living cells. Different vital staining and vital dissection methods (Kite,[27] Chambers[28]) have revealed interesting facts. Embryologic cytology and the mechanism of karyokinesis especially, have had new light thrown on them by this method. Among other methods may be mentioned the centrifugation of the early stages of fertilized eggs of lower animals, whereby light has been thrown not only on purely evolutionary mechanics, but also on the finer cytologic phenomena (Conklin, Lyon,[29] Lillie,[30] and others). In nerve cells, vital methods have not been so successful, because the nerve cell is usually too large and compact to permit the transmission of sufficient light; it cannot be studied uninjured under the microscope. The methylen blue method, even in such skilful hands as those of Ehrlich and Dogiel, has given only a limited knowledge of certain special cell constituents. Aside from the Nissl bodies, the most successful vital studies of the ganglion cell have been made on mitochondria (M. R. and W. H. Lewis,[31] Cowdry[32] and others).

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27. Kite, G. L.: The Relative Permeability of the Surface and Interior Portions of the Cytoplasm of Animal and Plant Cells, Biol. Bull. 25, 1912; Some Structural Transformations of the Blood Cells of Vertebrates, J. of Inf. Dis. **15**:319, 1914.

28. Chambers, Robert, Jr.: Some physical properties of the cell nucleus, Science, N. S. **40**:824, 1917; Lancet Clin., March 27, 1915; Microdissection studies: I. The Visible Structure of Cell Protoplasm and Death Changes, Am. J. Physiol. **43**:1, 1917.

29. Lyon, E. P.: Report of Centrifuging Eggs, Arch. f. Entwicklungsmech. **23**: 1907.

30. Lillie, F.: On the Specific Gravity of the Constituent Parts of the Egg of Choetopterus and the Effect of Centrifuging on the Polarity of the Egg, Science **27**: 1906.

31. Lewis, Margaret R., and Lewis, W. H.: Mitochondria (and Other Cytoplasmic Structures) in Tissue Cultures, Am. J. of Anat. **17**: 1914.

32. Cowdry, E. V.: Mitochondria and Other Cytoplasmic Constituents of the Spinal Ganglion Cells of the Pigeon, Anat. Rec. **6**:33, 1912; The Relations of Mitochondria and Other Cytoplasmic Constituents in Spinal Ganglion Cells of the Pigeon, Internat. Monatschr. f. Anat. u. Physiol. **29**:473; The Comparative Distribution of Mitochondria in Spinal Ganglion Cells of Vertebrates, Am. J. Anat. **17**:1, 1914; Vital Stain of Mitochondria, Internat. Monatschr. f. Anat. u. Physiol. **31**:267, 1914; Mitochondria and Neurofibrils, Am. J. Anat. **15**: 1914; The Mitochondrial Constituents of Protoplasm, Carnegie Institute, Washington, D. C.; Contributions to Embryology, **8**: No. 24, 1918.

Recently, the ultramicroscope, introduced into colloidal chemistry by Siedentopf and Zsigmondy, has proved useful. Marinesco [33] and Mott [34] have studied the protoplasm of the ganglion cell under the ultramiscroscope. Both state that the protoplasm is in a semifluid condition, with the granules that are always to be found in an emulsion by that method. The nucleus and nucleolus can be distinguished in the cell body, but further structural characteristics cannot be observed. A striking feature is the complete absence of a picture of the neurofibrils. Mott concludes that the neurofibril is probably an artefact produced by the fixation process. Marinesco states his conviction that, even if the neurofibrils are not to be seen in the ultramicroscope, yet they must exist preformed in the cell. Duesberg,[35] an experienced cytologist, asks, for other reasons, whether neurofibrils really exist in the cell. These quotations show that the existence of the neurofibril in the living cell has been questioned. Nothing concerning the morphologic constituents of nerve cells has seemed better established than our knowledge of the basophil or chromatophil bodies of Nissl. Ultramicroscopic studies have made their nature very questionable. Marinesco states that they cannot be detected in the living protoplasm. The bulky chromatophil masses which are the most conspicuous formations in the ganglion cell treated with ordinary staining methods must, from his studies, be considered as precipitates caused by the fixative. They exist in the living cell in a semifluid condition. A similar opinion had already been formulated by Held [36] and A. Fischer.[37]

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33. Marinesco, G.: Des changements qu'impriment à la luminosité et à l'état colloidales cellules nerveuses vivantes certains agents physiochimiques, Compt. rend. de la Soc. de biol. **70**:1061 (March 18) 1911; L'importance des phénomènes physio-chimiques dans la mécanisme de certaines phénomènes de la vie, Études ultramicroscopiques des cellules des ganglions spinaux des animaux nouveaux nés, ibid., p. 1057; Forschungen über die Kolloide der Nervenzellen und ihre erfahrungsgemässe Veränderungen, Kolloid Ztschr. **11**:209, 1912, and with Minea, J.: Récherches sur les métamorphoses neurofibrillaires des fibres nerveuses périphériques sectionnées, Ann. d. biol. **1**:1057, 1911; Etudes des cellules des ganglions spinaux de grénouille à l'aide de paraboloide de Zeiss, Rev. d. 1. Soc. de biol. **71**:202 (June 22) 1911.

34. Mott, F. W.: The Bio-Physics and Bio-Chemistry of the Neurone, Brit. M. J. **2**:786 (Sept. 28) 1912.

35. Duesberg, J.: Trophospongium und Golgischer Binnenapparat, abstracted in Anat. Anz. **46**: 1914; On the Present Status of the Chondriosome Problem, Biol. Bull. **36**: Pt. 2 (Feb.) 1919.

36. Held, H.: Beiträge zur Struktur der Nervenzellen und ihrer Fortsätze, Arch. f. Anat. u. Physiol. p. 204, 1897; ibid., supplement, p. 273.

37. Fischer, Alfred: Zur Kritik der Fixierungsmethoden und der Granula, Anat. Anz. **9**:678, 1894; Fixierung, Färbung und Bau des Protoplasmas, Jena: 1902.

Finally, the interesting intracellular canals, the trophospongium of Holmgren,[38] can be studied in the living cell by the use of vital staining (Cowdry), but the real nature of this apparatus is still doubtful. The relation between these canals and the exterior of the cell, whether the canals have walls of their own, and what is the physiologic nature of their contents, are still important questions concerning which no agreement is to be found in the literature.

The writer has investigated some of these problems by the study of the histology of the ganglion cells after centrifugation. By this method it was hoped to produce an alteration of the mutual interrelation and arrangement of the cellular constituents. The method would reveal whether there is a difference in the specific gravity of different cell parts, and give information on the physical nature of the cytoplasm and problems of viscosity. The centrifugation would act, as already suggested, as a means for endocellular dissection of the living cell.

MATERIAL AND METHODS

For cytologic studies, the spinal ganglions of rabbits were removed immediately after death induced by chloroform, and were tied up in the adherent nerves with ordinary sewing thread. They were then put into centrifuge tubes, suspended in blood serum from the same animal, and the tubes were rotated at a speed of approximately 3,000 revolutions per minute. The duration of the centrifugation varied from fifteen minutes to three hours, the upper limit being chosen in reference to postmortem changes in the tissue.

The immersion of the ganglions in the serum was intended to keep them in natural surroundings and to postpone death. In the meantime, it was found that the effect of centrifugation could be increased by leaving the preparations hanging freely during the procedure, with a small amount of serum at the bottom of the tube. Centrifugation under these circumstances had, of course, a drying effect on the ganglions, as water was forced out from the tissue. The histologic effects of this were limited to the external cell layers of the ganglion, and the experiment could no longer be regarded as a centrifugation of living cells. The whole ganglion, hanging freely in the tube, was considerably stretched during the centrifugation and the cells within the ganglion were exposed to considerable pressure on account of this stretching.

38. Holmgren, Emil: Zur Kentniss der Spinalganglienzellen von Loph. piscatorius, Anat. Heft. **12:** Pt. 38, 1899; Weitere Mitteilungen über den Bau der Nervenzellen, Anat. Anz. **16:** Pt. 15-16, 1899; ibid., **17:** Pt. 6-7, 1900; Studien in der feineren Anatomie der Nervenzellen, Anat. Heft. **15:** Pt. 1, 1900; Weitere Mitteilungen über die Saftkanälchen der Nervenzellen, Anat. Anz. **18:** Pt. 11-12, 1900; ibid., **20:** Pt. 18, 1902.

Nevertheless, the results of these experiments proved interesting and valuable.

Ganglions from the crab were treated in the same way. Experiments were also made on the frog. The entire central nervous system was cut out in one piece, still enclosed within the skull and the vertebral canal. The whole piece was put into the tube and centrifugated. When the cranial cavity was opened afterward, it was found that the neuraxis had been thrown by the centrifugal force into its distal part, was more or less deformed and was compressed into smaller bulk.

Pieces of the spinal cord and brain of rabbits, obtained immediately after the animals had been killed, were also subjected to centrifugation. The pieces were placed in a centrifuge tube for this purpose. The centrifugation brought about a severe deformation of the loose tissues which interfered with later histologic examination. The ganglions of the crab were cut out and suspended in the centrifuge tube in the way described above for the spinal ganglions of the rabbit.

The entire skull of the mouse, immediately after decapitation, was submitted to centrifugation. The skulls could be put in different positions in the tube in order to bring about different directions of the centrifugal displacement in the tissues. After centrifugation, the brain within the skull was found macroscopically intact. There was no marked deformation of the tissues, and the only effect was the cellular change to be described later.

The staining methods used were: alum-hematoxylin-van Gieson for general survey and Nissl's methylene blue for the chromatin bodies; Kopsch's osmium method for the intracellular canalicular apparatus; the Cajal and Bielschowsky methods of silver impregnation for the intracellular canalicular apparatus and neurofibrils. The tissues were cut in the plane in which the centrifugal force had acted on them. In the description of the sections, the terms "distal" and "proximal" will be used to designate the direction of the centrifugal force; the center of the centrifuge will be called "proximal" in relation to its "distal" periphery.

RESULTS OF EXPERIMENTS

The experiments that gave only minor tissue deformation will be described first. Those in which the entire skulls of mice had been centrifugated showed the most surprising results. The distal vessels were filled with blood, suggesting an hyperemia, otherwise the brain, protected by the skull, had preserved its configuration. In other words, there was no gross anatomic lesion of the brain substance. Histologically, there was widespread displacement of the nuclear constituents. In the majority of the cells the nucleolus was displaced distad, and there was

evidently fractioning of the entire nuclear contents, which had accumulated at the distal pole of the nucleus. In the proximal part of the cell the whole nuclear contents seemed to be displaced distad, so that the proximal end appeared like a vacuole; the chromatin threads of the nucleus were apparently torn asunder in its proximal part.

These nuclear changes were found in all parts of the brain. In some regions there were a number of cells in which the nuclear substance seemed intact, but, for the most part, the effect was widespread. The change in the cortex was the same as in the basal ganglions. In the cerebellum, all the nucleoli of the Purkinje cells were thrown in the same direction, and the same changes were present in the granular layer of the cerebellar cortex.

No certain alterations could be detected in other parts of the cells; the nucleus had maintained its normal shape and position in the cell; and no displacements of the tigroid bodies could be demonstrated. Concerning the fibrillar net, the Bielchowski preparations showed no definite deformations; but the nuclear content showed very evident changes, as is illustrated by the figures. No certain displacements could be shown in the spatial relations of different brain regions; gray and white matter seemed to have conserved their structure as far as the histologic examination revealed. The fiber web of the nervous system seems to form a firm, strong entanglement which retains the cells in situ even after exposure to such forces as centrifugation. This, of course, does not exclude the possibility that they have suffered a tension that would interfere with their function.

On the whole, I have been able to confirm the statements of Arndt that the nucleoli are very sensitive to centrifugation. But, in opposition to this author, I have not found displacement of the nucleus within the cell. I must agree with him when he says that "die Befestigung von Zelle und Kern in ihrer Umgebung von erstaunlicher Vollkommenheit sein muss."

Similar changes were observed after centrifugation of the frog's brain enclosed in the intact skull. Here, also, in all nuclei the nuclear substances were thrown distad. The same result was obtained after centrifugating ganglions from the crab. Centrifugation of the pieces of the nervous system of the rabbit also showed similar results, but here a coarse deformation, due to pressure of the brain mass into the tube, had brought about an alteration of the tissue that interfered with histologic examination.

Pieces of human medulla oblongata that had been exposed to the same treatment showed none of the changes described. The pieces could not be obtained until several hours after death, and it is assumed that postmortem coagulation had already taken place, and that this coagula-

tion had increased the viscosity of the tissue so that no effect was produced by the centrifugation.

The spinal ganglions exposed to centrifugation in the manner described also showed many signs of coarser deformation, owing to the fact that during the experiment they were exposed to physical influences of various kinds (drying, tension and pressure). The most normal mac-

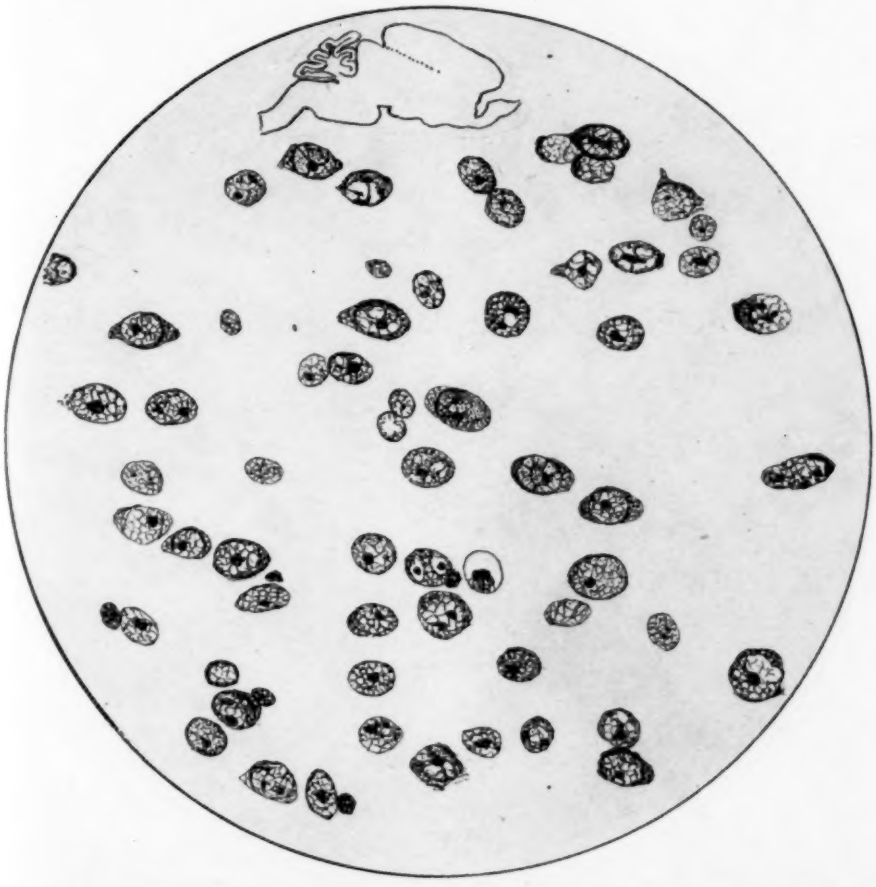

Fig. 1.—Normal arrangement of the nuclear contents in a mouse's brain. Haematoxylin-eosin. Zeiss Obj. 2 mm., Ok. 4.

roscopic configuration was shown by the ganglions which had been immersed in serum. Here the cells were rounded in the normal manner. No certain displacement of the cytoplasmic constituents nor of the nucleus itself could be demonstrated. That the nucleus was not moved indicates that it is firmly enmeshed and suspended in the fibrillar net of the cytoplasm within the cell.

A never-failing phenomenon observed in the centrifugated cells was the excentric position of the nucleoli, close to the nuclear membrane at the distal pole of the nucleus. This phenomenon was observed after fifteen minutes' centrifugation, when no other effects could be detected. It was still more marked in preparations rotated for two hours. But, even in the preparations run the longest time, the nucleolus was seldom found in contact with the nuclear membrane.

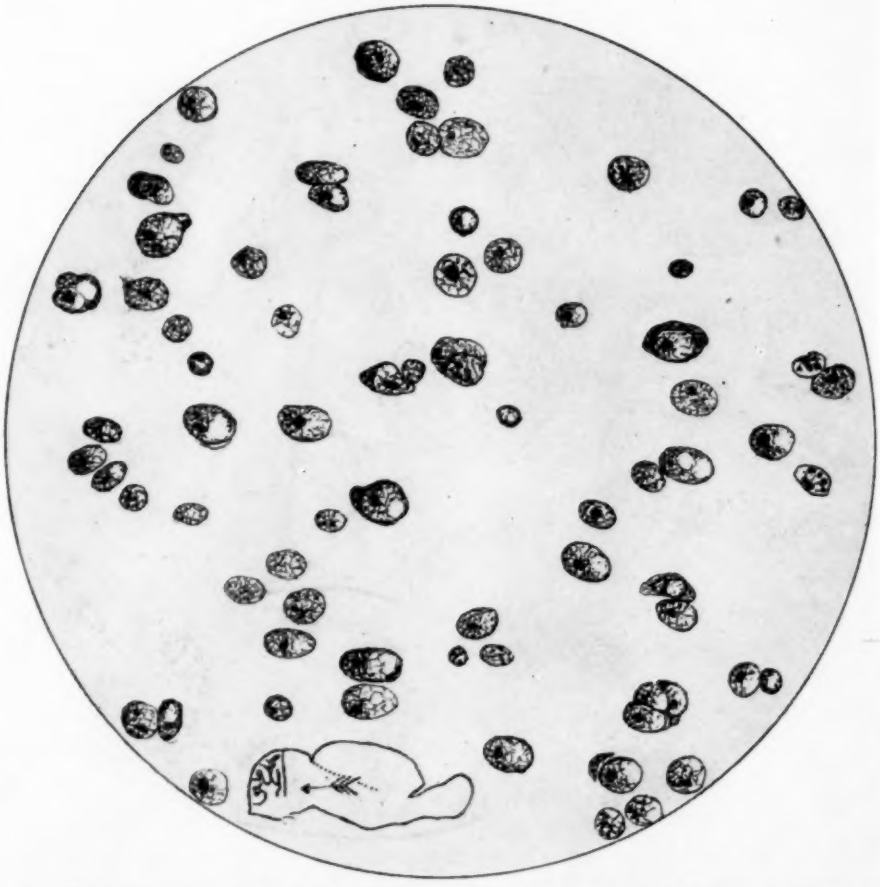

Fig. 2.—Arrangement of the nuclear contents in a brain of a mouse, the skull of which had been centrifugated for forty-five minutes in a centrifuge with a speed of about 4,000 revolutions a minute. The arrow indicates the direction in which the centrifugal force has acted. Haematoxylin-eosin. Zeiss Obj. 2 mm., Ok. 4.

The conclusion from these findings is that the nucleus of the ganglion cell is a vesicle, filled with a fluid of comparatively low viscosity, in which the nucleolus and other contained structures are movable in any direction by external physical forces. Closer to the nuclear membrane,

the nuclear content increases in density, and thus prohibits the nucleolus from coming in actual contact with the membrane. The low viscosity in the nucleus in even such a highly specialized cell as the ganglion cell becomes more interesting in consideration of the fact that, as Herrick [39] found in developing eggs of the lobster, the nucleoli settle to the bottom of the nuclei by gravity.

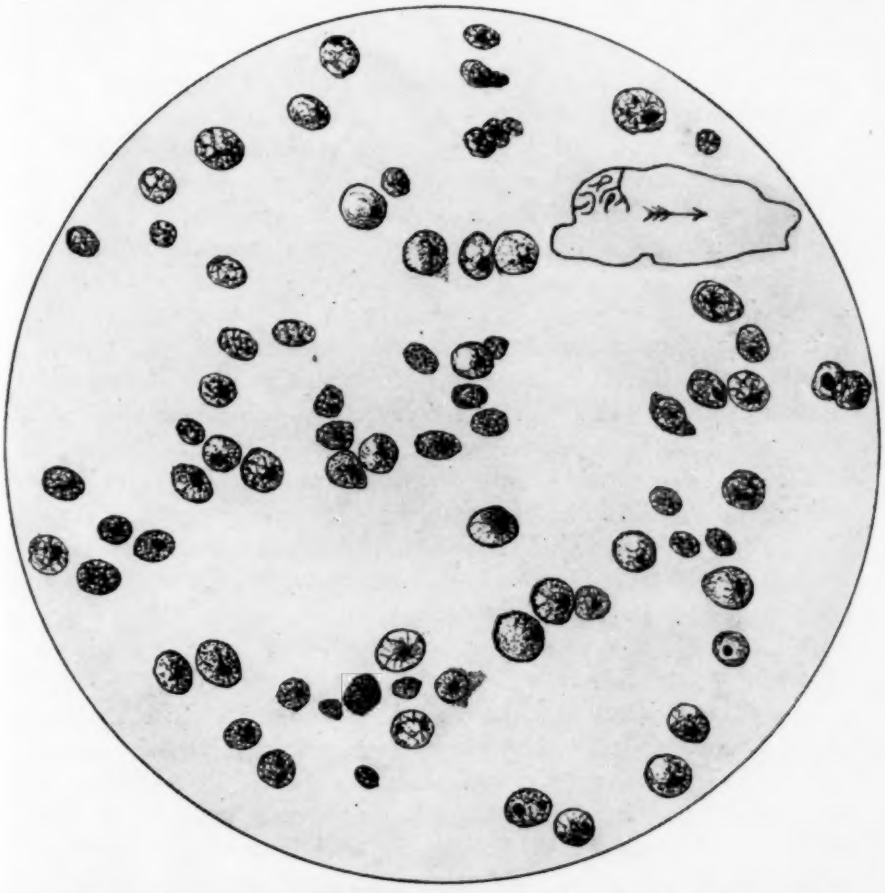

Fig. 3.—Arrangement of the nuclear contents in a brain of a mouse, the skull of which had been centrifugated for forty-five minutes in a centrifuge with a speed of about 4,000 revolutions a minute. The arrow indicates the direction in which the centrifugal force has acted. Haematoxylin-eosin. Zeiss Obj. 2 mm., Ok. 4.

In the experiments in which the spinal ganglions of rabbits had been centrifugated hanging freely in the centrifuge tube, the phenomena

39. Herrick, F. H.: Movements of the Nucleolus Through the Action of Gravity, Anat. Anz. **10**:337, 1895.

within the nucleus already described were always found. In addition, a series of deformations was noticed, indicative of the various kinds of influences that had acted on the ganglions (drying, stretching and centrifugal force). These deformations, in many instances, were so intense that they must have had a severe effect on the cells, and the observations have, therefore, no bearing on the living cell.

The alterations of the ganglion cell as a whole consisted of a change of the cell shape from the characteristic rounded form to a more regular ovoid, which, in highly deformed cells, became an irregular ovoid with the proximal end more or less pointed and the distal end blunt. On the whole, the most marked effects were to be seen in the peripheral layers of the ganglion, and were probably due to a combination of two mechanical factors—pressure and centrifugal force.

In the protoplasm itself, no effect was to be seen in preparations run in the centrifuge less than one hour. When run more than an hour, it could be seen that the Nissl bodies gradually collected at the distal pole of the cell. Various degrees of this process were observed. In some, a thin sheet of chromatophil bodies covered the distal pole like a crescent; in other cells, there was a general condensation of the chromatophil substances in the distal half of the cell; in others, at the distal pole, there was a large irregular clump of chromatophil substance, the rest of the cell being devoid of it. In the cells that were most deformed and pressed together, the chromatophil bodies were gathered in clumps at both ends of the cell. The chromatophil substances at the proximal end of the cell must be considered as probably brought there by the squeezing of the cells from the sides.

The deformation was often irregular. One cell might give an apparently normal picture, while a neighboring cell was highly deformed. This undoubtedly indicates that the physical state of the cell content varies in different cells within the same ganglion. The deformations, and especially the changes brought about in the chromatophil substances in the cells, make it probable that those substances exist in the living cell in a fluid condition. As will be explained later, the movements of these substances through the neurofibrillar framework cannot be explained in any other way. These results thus conform with the findings of Marinesco,[33] Mott [34] and others with the ultramicroscope.

The intracellular canals in centrifugated cells show interesting features. In cells without deformation of shape, the canalicular apparatus appeared normal. This was true even when a marked effect was to be seen on the nucleus and the position of its nucleolus. Even when general distortion of the whole cell toward the ovoid form occurred, no deformation of individual canaliculi could be detected. As, under such conditions, this apparatus must be exposed to a tension sufficient

to give the whole cell another shape, the maintenance of the form of the canalicular apparatus indicates that its contents are incompressible and have no easy way of escaping when pressure is exerted on the cell. Still more interesting conclusions can be drawn from the cells that exhibited the greatest degree of changes. In these, at the distal end of the cells, among the chromatophil masses outside the neurofibril system, the canalicular apparatus was to be seen in the form of irregular droplets or curved rods. Here, to a certain degree, there had occurred a limited confluence of the different canaliculi. Furthermore, there was apparently no confluence or mixture of the two substances—the chromatophil substances and the contents of the canaliculi. Thus, even after it has been squeezed from its natural position in the cell, the canalicular system preserves, to a large extent, its morphologic character. This leads to the conclusion that the contents of the canaliculi must have a relatively high degree of viscosity. If, with Holmgren, one assumes special differentiated walls for this canalicular system, these walls must be assumed to undergo ruptures in the squeezing process. The experiments show that apparently, even after such ruptures, this substance maintains physically and chemically its natural structure.

Further studies, especially with the application of Holmgren's elaborate methods for this special apparatus, will undoubtedly yield interesting information on the nature of this canalicular apparatus, especially with regard to the question of its walls and extracellular connections.

The neurofibrillar net shows changes of great interest in the centrifugated cells. In the more moderately deformed cells, when the chromatophil substances accumulated in a crescent at the distal end, no neurofibril net was found in this part of the cell. This net has apparently less elasticity than other structures and resists the squeezing process, so that the chromatophil substances and the canalicular apparatus are forced out of it. The more the ganglion cell was stretched by the centrifugal action, the more the neurofibrillar net system became loosened from the cell membrane and retracted to the center of the cell as an ovoid field containing the nucleus with its nucleolus.

This relation of the neurofibrillar net to the nucleus gives the impression that these parts form a morphologic unit. This is the more interesting when one takes into consideration the fact that recent investigators into the origin and development of the neurofibrils have shown that they arise in some way from the nucleus (Gerini,[40] Cowdry,[32]

40. Gerini, Cesare: Quelques récherches sur les prémières phases de développement des neurofibrilles primitives chez l'embryon du poulet, Anat. Anz. **33**:178, 1908.

and others). The experiments show conclusively, I think, that, contrary to the doubts expressed by several authors, the neurofibrils exist preformed in the living cell. If we suppose that the fibrillar structure observed in the oval field within these cells is an artefact, produced by the fixation fluid, we must assume that this same oval field before fixation of the centrifugated cell was made up of a special substance, which usually gives the structure of this characteristic feature of the nerve cell. We must also assume, then, that this fibrillar substance has, in a concentrated form, been retracted to the center of the cell. But, in such case, it is impossible to account for its regular oval form. This can be explained only by the supposition that the neurofibrillar skeleton in the cell has—apparently owing to its relatively slight elasticity—not been able to adapt itself to the deformations of the other cell constituents, but has, as a unit, become loosened from the cell membrane and retracted to the center. In other words, the nerve fibril is preformed in the living cell, and is apparently one of the most important cellular organs within the nerve cell.

COMMENTS

The experiments show conclusively that a physical force, which acts indirectly on the nerve cells, brings about conspicuous displacements of the different parts within the cell owing to differences in specific gravity. Probably this is a widespread effect on all cells of the nervous system as well as of other organs. Such displacements cannot be irrelevant to the functions of the cells. They must cause profound alterations of the dynamic state of the cells (electrical double-layer on the membranes, surface tension of the different colloids, etc.). Probably in more advanced degrees they mean complete abolition of function.

In this way undoubtedly many symptoms of loss of function in commotion might be explained. Severe traumatism to the skull must bring about a concussion of the neuraxis and its cells. Ruptures of vessels with hemorrhages and lacerations of the nervous substance (contrecoup) may occur, but to these must be added the endocellular effects of the violence. The latter alone may be responsible for the fatal issue in cases of death during the acute stage of the commotion, in which no manifest anatomic lesions have been detected. Such alterations in the vital centers in the medulla oblongata (Huet and others) must be considered highly dangerous and liable to cause sudden death after a blow against the skull.

The physical force must be considered to act on all cells in the nervous system, and we recognize that a great variety of symptoms may be exhibited by victims of traumatic shock which indicate widespread lesions (loss of consciousness, deafness, blindness, sensory disturbances, tremor, ataxia, choreatic movements, hemiplegia, aphasia, etc.). Most

of these symptoms may seem grave in the acute stage, but they often vanish completely within a short time after the injury. This rapid regression of the commotional symptoms is easily explained by assuming the mechanism for these lesions that has been described. It may be supposed, at least in the lesser degrees of endocellular displacement, that the cell is able to make a comparatively rapid recovery. On the other hand, it does not seem improbable that more advanced displacement may lead to death of the cells, and in this way to many of the degenerative phenomena [23] observed in the chronic stages of commotion. Widespread endocellular displacements in the brain seem to me to be likely to elucidate some of the psychic symptoms in commotion (amnesia, dulness, general retardation, psychotic signs, exaltations, manic excitement, etc.), in cases in which an emotional genesis of these symptoms can be excluded. I think that the traumatic endocellular displacements demonstrated in these experiments cannot be considered to be unrelated to the genesis of many of the symptoms of the traumatic neuroses.

It has been stated by several authors that the symptoms of spinal commotion suggest hematomyelia. Roussy and l'Hermitte are skeptical of this and emphasize the fact that the syndrome indicates a lesion of the gray matter. This finds a natural explanation in the centrifugation experiments, which have shown that the most conspicuous changes are within the cells, whereas the fibers of the white matter present no visible signs of such alterations.

Tillman, during his experimental studies, found that commotion was more likely to follow when the head of the animal was either struck against a wall or was dealt a severe blow when held freely. But a blow dealt while the head was held against a firm support did not have a commotional effect. These observations and statements by Tillman, which have not been without criticism, find an explanation in the results of the experiments here reported. If the skull at the moment of impact is resting against a solid foundation, the physical force cannot operate on the contents of the skull in the same way as it can when the skull can be moved freely by the blow. Thus the cellular changes which are the cause of commotion will appear especially when the skull can be moved freely.

Apparently the alterations demonstrated in cells that have been exposed to centrifugation might be ranged with the so-called molecular lesions. This term cannot be considered adequate in a strictly physical sense, as there is no displacement of the molecules of the protoplasm. The displacement within the cells is a displacement of conglomerates of molecules, and is due to differences in specific gravity. The first question that arises is whether the displacements observed in the centrifugated brains can in any respect be compared with changes brought

about by the physical factors that usually lead to commotion. Certainly they cannot be compared directly. But the centrifugal changes undoubtedly show that a physical factor acting indirectly on the cell is able to produce changes in the cell.

The experiment of centrifugating the cells affords the advantage that the force imposed on a given particle of the cell can be compared exactly with a force of known velocity acting on the skull. Undoubtedly many traumatisms act on the cellular constituents with a force that is many times stronger than that used in the experiments. Carver and Dinsley [3] state that the compression waves of detonations act with a speed of about 10,000 meters per second. If such a terrific force is imposed on the skull, it must necessarily produce, in addition to other damage, severe and widespread cellular changes of the type described above.

The physical effect of traumatism against the skull is undoubtedly intricate. The violence will impose its energy on the skull as a whole, but owing to the elasticity of the skull there will, in many cases, also be a local impression of the bones that will act on the cranial contents as a "decompressive cone." The contrecoup effect must be given consideration, and sudden movements of the cerebrospinal fluid may undoubtedly cause tensions or lacerations in parts of the brain. But, among all these highly complex alterations, the cellular changes of the type described in this article are undoubtedly largely responsible for the widespread loss of function of the more severe cases of commotion.

SUMMARY AND CONCLUSIONS

Prolonged intense centrifugation of living ganglion cells can bring about a separation of the cell constituents, or an alteration of their mutual interrelations. This has a bearing on the effects of severe trauma—concussions and other physical forces—on the nervous system. It supports strongly the assumption that direct cellular disturbances are the cause of many acute commotional symptoms.

The part of the ganglion cell that can be most easily moved within the cell by centrifugation is the nucleolus. After a short centrifugation this is always thrown to the distal end of the nucleus and proves that this latter is a vesicle, the contents of which have a low viscosity.

The next most conspicuous change after centrifugation consists in an accumulation of the chromatophil substances at the distal end of the cell, and proves that these bodies must exist in a fluid condition in the living cell. This accords with the observations on the living cell with the ultramicroscope.

The canalicular apparatus is squeezed out of its position in the cell by centrifugation, but maintains its normal morphologic character; this

demonstrates that the contents of this apparatus do not mix with the chromatophil substances and that they probably have a high viscosity.

The neurofibrils show less elasticity than surrounding constituents and can be separated from other parts of the cell. The whole net of neurofibrils loosens as a unit from the cell membrane and, when centrifugation has been sufficiently strong, occupies the center of the cell and encloses the nucleus. This proves that the doubts raised in modern histologic literature as to the neurofibrils are not justified; the neurofibrils exist in the living specimen and are not artefacts brought about by fixative agents.

HISTOLOGIC CHANGES PRODUCED EXPERIMENTALLY IN THE CENTRAL NERVOUS SYSTEM OF MONKEYS BY MERCURY*

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PHILADELPHIA

In previous papers on the histologic changes produced experimentally in rabbits and rats by arsphenamin, neo-arsphenamin and mercury[1] we have reported certain lesions in the central nervous system of these animals, which may be summarized as follows: Multiple doses of the arsenicals, in excess of the calculated therapeutic amounts, produced hyperemia, focal hemorrhages, some endothelial proliferation and, frequently, hyaline or conglutination thrombosis. After multiple doses of the mercurials, the most striking findings were, in a considerable number of rabbits, a perivascular and pial small round cell infiltration. This later lesion had not been observed in the numerous control animals nor in those treated with the arsenicals, and was therefore regarded as being induced by the mercurials used. We felt, however, in view of the importance of the subject, that these experiments should be repeated, and we selected monkeys because of their closer phylogenetic relationship to man. An added reason for

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* From the McManes Laboratory of Pathology of the University of Pennsylvania, and the Research Institute for Cutaneous Medicine, Philadelphia.

* Investigation aided by a grant from the Research Institute for Cutaneous Medicine, Philadelphia.

1. Kolmer, J. A., and Lucke, Baldwin: A Study of the Histologic Changes Produced Experimentally in Rabbits by Arsphenamin, Arch. Dermat. & Syph. **3**:483, 1921; A Study of the Histologic Changes Produced Experimentally in Rabbits by Neo-Arsphenamin, ibid., p. 515; A Study of the Histologic Changes Produced Experimentally in Rabbits by Mercurial Compounds, ibid., p. 531.

this selection was that the objection has been raised that spontaneous lesions in the various organs of the rabbit are of not infrequent occurrence.[2]

MATERIALS AND METHODS

Preliminary to the experimental study, twenty-two brains from primates which had died at the Philadelphia Zoological Garden were investigated. It was found that spontaneous lesions were not uncommon, but no tissue changes simulating those to be described were encountered.[3]

For the experiments, three rhesus monkeys, in good condition, were used. They received mercurial treatment for three months as summarized in the accompanying table. All the animals lost weight

Mercurial Treatment of Monkeys

No.	Compound	Route of Administration	Dose, Gm. per 60 Kg.	Doses per Week	Total No. of Doses	Weight in Grams	
						Before Treatment	After Treatment
1	Mercurial ointment	Inunction	4	3	37	1,120	1,015
2	Bichlorid (in aqueous solution)	Intramuscular injection	0.02	3	37	2,400	2,075
3	Salicylate (in oil suspension)	Intramuscular injection	0.06	1	14	2,220	2,170

gradually, but showed no other clinical changes. After completion of the course of treatment they were killed instantly by decapitation. Blocks from various parts of the brain and cord were fixed in 95 per cent. alcohol and in Zencker's fluid. Paraffin sections of the former were stained with cresyl-violet and toluidin-blue; the Zencker material was stained with Mallory's neuroglia stain (phosphotungstic acid hematoxylin). The visceral organs were fixed in 10 per cent. dilution of liquor formaldehydi, embedded in paraffin, and stained with hematoxylin-eosin.

2. We have communicated with a number of investigators regarding the spontaneous occurrence of cellular infiltration in the nervous system of rabbits, and received diverse opinions. Some state that they have observed such changes in "normal" rabbits, while other equally qualified workers have never seen perivascular or meningeal round cell infiltration in any but experimental animals. After this paper was completed an article appeared by Jean Oliver on "Spontaneous meningeal and perivascular round cell infiltration in rabbits" (J. Infect. Dis. **30**:91, 1920). Oliver found this condition rather prevalent, but stated that Dr. E. C. Dickson, in 1917, using rabbits from the same stockroom, examined sixty experimental animals without encountering the lesions. Judging from his paper, and certain other data, this disease appears very irregularly distributed. We, ourselves, have recently found such lesions in rabbits not previously used in some investigation and we are now conducting a further study along these lines; until this is completed we reserve comments.

3. Lucke, Baldwin: Spontaneous Cerebral Lesions in Monkeys, Arch. Neurol. & Psychiat. **10**:212 (Aug.) 1923.

RESULTS

There were no gross lesions in the central nervous system. The histologic changes in the three monkeys were of similar character, but somewhat more marked in the animals receiving intramuscular injections than in the one receiving inunctions.

1. *Pia-Arachnoid.*—The pia-arachnoid was moderately thickened, and presented conspicuous cellularity; this was especially marked in the pial prolongations (Figs. 1 and 2). The collagenous fibrils were greatly increased in quantity, and here and there formed dense layers. The vessels uniformly possessed prominent endothelial and adventitial cells. The former, particularly, were

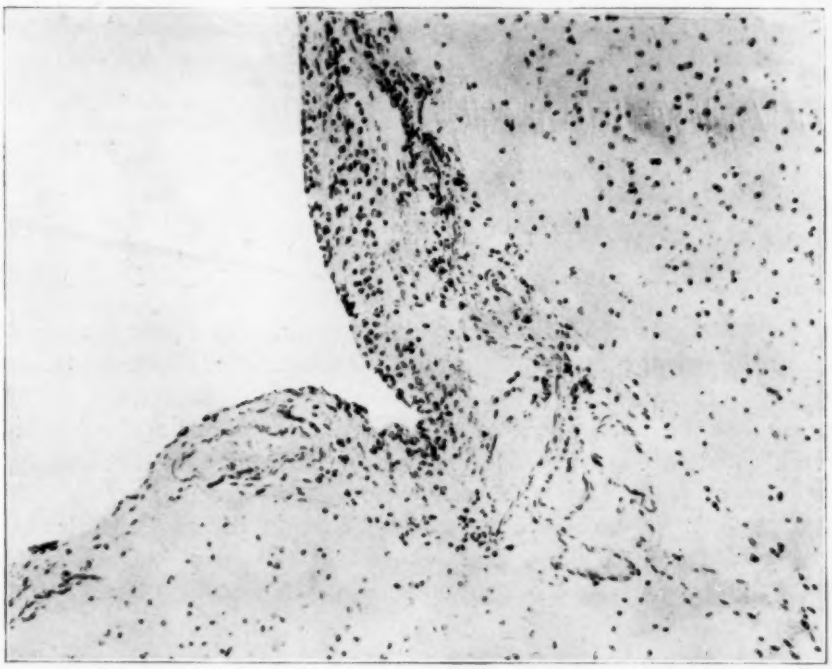

Fig. 1.—Pia-arachnoid over lower portion of occipital lobe, Monkey 3. The pia is moderately thickened and cellular, particularly in its prolongation.

actively proliferating, and stood out as prominent, oval, richly chromatic nuclei, taking a deep tint. Here and there they were heaped up, forming vascular buds. Quite a number exhibited retrogressive changes, their chromatin being condensed at the nuclear periphery; an occasional nucleus appeared fragmented.

The adventitial cells were likewise much swollen, very numerous, and apparently extended beyond the vascular boundaries. The pial cellularity was largely due to great numbers of young fibroblasts possessing blunt, oval, densely chromatic nuclei and elongated cell bodies. In addition there were many paler and larger nuclei with coarse chromatin dots at the periphery and scattered through the nuclear body; a distinct nucleus was present. These elements occurred in groups, and probably were derivatives of the arachnoid. Some very large

cells, with poorly stained, scanty cytoplasm and with a pale nucleus dusted with chromatic fragments, were difficult to classify and probably were degeneration forms of one or other of the cell types mentioned. A few round cells with a very deeply stained nucleus and almost no protoplasmic rim, probably belonged to the lymphocytic series. Lastly, many fragmented and broken-up cells were present; most often they appeared as collections of chromatin fragments arranged in an imperfect ring. Typical plasma cells and polymorphonuclear leukocytes were entirely absent. The cells present nowhere extended beyond the limiting glia. A curious picture was found in the cerebellar pia of Monkey 2. In addition to the thickening and cellularity, there were several irregular, partly hyalinized areas, thickly infiltrated with lime salts.

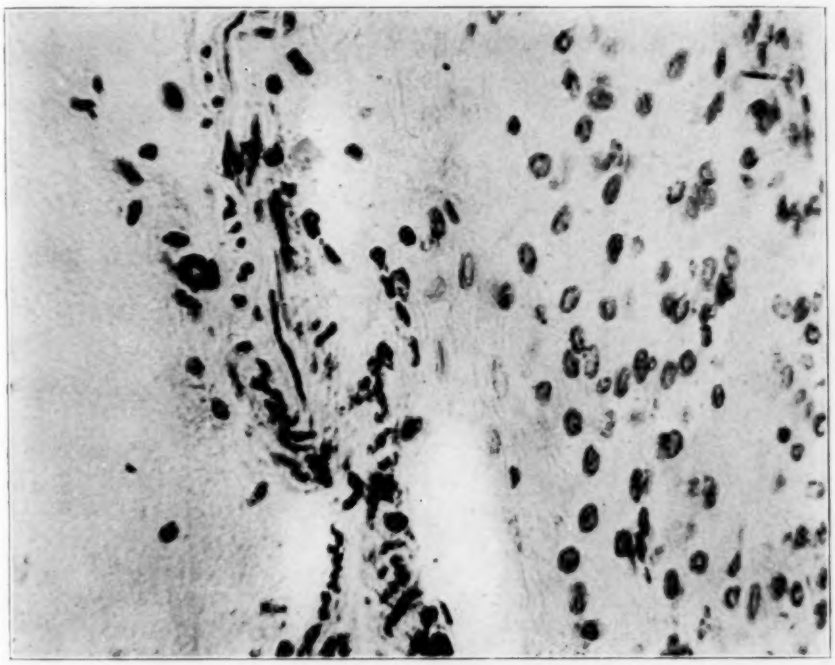

Fig. 2.—Higher power photomicrograph of the left portion of the section illustrated in Figure 1. The paler oval nuclei are chiefly fibroblasts; the collagenous fibrils are not well shown in the picture, but are very evident in suitably stained preparations. The illustration shows some degenerative elements; the various cell forms are discussed in the text.

The larger vessels in the various sections presented no noteworthy changes. Occasionally a splitting and fibrillation of the internal elastica was seen, but since cerebral arteriosclerosis, as we have shown, appears to be of not infrequent occurrence in monkeys, we are inclined to regard this condition as independent of the experiment. On the whole the pial changes were more marked on the basal portions of the brain; they often appeared particularly pronounced over the cerebellum. The pia of the cord was only moderately and locally involved. Indeed, it is to be emphasized that the productive alterations described were not a diffuse, but a localized process.

2. *The Vessels of the Brain and Cord.*—Marked proliferative changes were present in the blood vessels, particularly in their smallest branches and in the capillaries. Their endothelium was much swollen, abundantly chromatic, stained deeply, and showed evidence of multiplication. Thus, vascular buds were frequently found (Figs. 3 and 4). Even the smallest capillaries stood out boldly, and newly formed branches, tapering to a point, were much in evidence. The adventitial cells were likewise swollen. The Virchow-Robin spaces were, as a rule, distinct and in a number of instances contained foreign cells. This infiltration was never great, and the cells were usually difficult to group (Figs. 5 and 6). A few conformed to the typical picture of plasma cells; they pos-

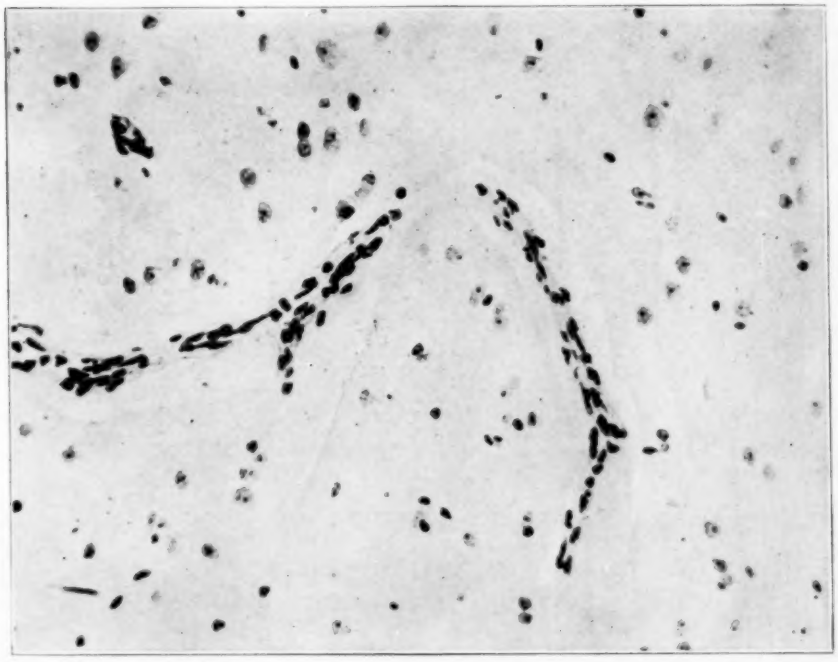

Fig. 3.—Central lobule of Monkey 3. The two small vessels show very prominent endothelial and adventitial cells, and bud formation.

sessed a rounded, somewhat eccentric nucleus, with characteristic wheel-like arrangement of the chromatin, a clear nuclear court, and, usually, a somewhat basophilic cell body. Some deeper staining, more diffusely chromatic nuclei, of smaller size and with a scanty cytoplasmic rim, were regarded as lymphocytes; the rest of the cells were intermediate forms and degenerating elements. Of the latter the most noteworthy type possessed a large nucleus and a pale spongy cytoplasm; these were probably reticulated (Gitter) cells. It is to be emphasized that the adventitial sheath infiltration was always scanty, and occurred in a relatively small proportion of the vessels. It never consisted of more than one layer of cells and did not extend beyond the limiting glial membrane (Fig. 7). Somewhat confusing was the occurrence of a "pseudo

round cell infiltration," occasioned by the tendency of proliferating neuroglia cells to group themselves about the periphery of the vessels. This will be discussed further below.

In some capillaries degenerative changes were observed. The lining cells were greatly swollen, very pale in their staining characteristics, poorly chromatic, and indistinctly outlined; sometimes the capillary lumens appeared obliterated. Frequently the entire visible part of the vessel presented this degeneration, but sometimes only rare cells were involved. The larger vessels exhibited far less pronounced proliferation and degeneration. Their endothelium was only mildly swollen, not heaped up, the lumen was never narrowed

Fig. 4. Central lobule of Monkey 3. The photomicrograph shows a capillary with markedly swollen endothelium and early bud formation. The cell bodies of the proliferating cells are somewhat granular; the adventitial cells are likewise enlarged.

and there were no distinct changes in the elastica or muscularis. In connection with the vessels must be mentioned the presence of small numbers of sausage-shaped, elongated, blunt ended nuclei, sometimes staining deeply and at other times faintly, which possessed a scanty, somewhat fibrillar protoplasm. These rod (Stäbchen) cells, at times seemed to spring from the adventitia, but often had no apparent relation to blood vessels and occasionally appeared to be of glial origin. They were present with equal infrequency in the gray and white matter.

The vascular changes outlined were very irregularly distributed, but they were most pronounced in the white matter of the basal portions of the brain.

In the brain stem and the cord they were least marked; the cortex occupied an intermediate position. Exceptions to this general statement were frequently observed.

3. *The Neuroglia.*—There was a moderate but distinct proliferation of the cellular as well as the fiber-forming neuroglia. The latter was best seen in the subependymal and marginal cortical layers, and encircled the vessels, that is, it occurred in places where normally the fibrils are best developed. The cellular glia exhibited particular proliferation about certain small blood vessels. Here irregular rows and groups with abundant protoplasmic processes were much in evidence. The nuclei were hyperchromatic and extraordinarily large, the cell bodies clearly defined for considerable distances. Throughout many

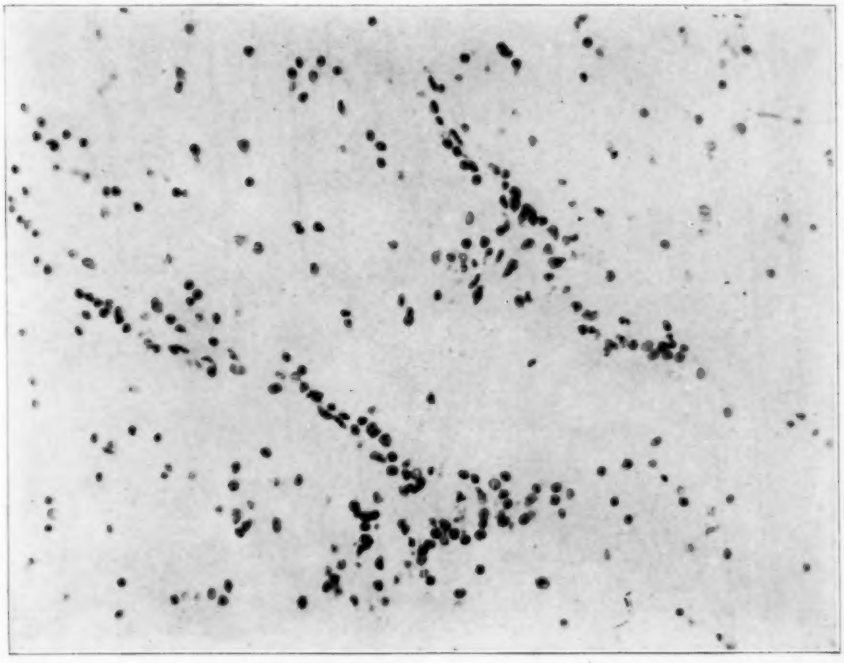

Fig. 5. —Centrum ovale of Monkey 1. Two small vessels with prominent lining cells and bud formation are shown. There is a mild infiltration in the adventitial sheath with round cells.

portions of the white matter there were long chains and groups of similarly proliferating neuroglia, their bodies frequently fused. Occasional doubtful mitotic figures were present. In the cortex the glia was less distinct, but groups of such cells often surrounded degenerated ganglion cells and sometimes they replaced lost portions of these elements. Degenerative changes in the glia were not infrequent. They manifested themselves chiefly by great paleness of the ballooned nucleus, disappearance of nucleolus and nuclear membrane, and by fragmentation. Chromatin débris, undoubtedly of glial origin, was often found.

4. *The Ganglion Cells.*—There was no disturbance of the cortical architecture, but degenerative changes were occasionally observed. The most common type consisted in swelling of the cell body, with loss of clear outline and vacuolization; the nuclei were frequently eccentrically placed, the processes swollen and traceable for a considerable distance. In other types the nucleus or portions of the cytoplasm had disappeared; chromatolysis was fairly common. So-called chronic changes were only rarely seen. There was no tortuosity or thickening of the processes, and no incrustation with lime salts. The distribution of ganglionic changes was irregular. These degenerations must be regarded as of antemortem origin in view of the fact that the tissues were fixed immediately after killing the animal.

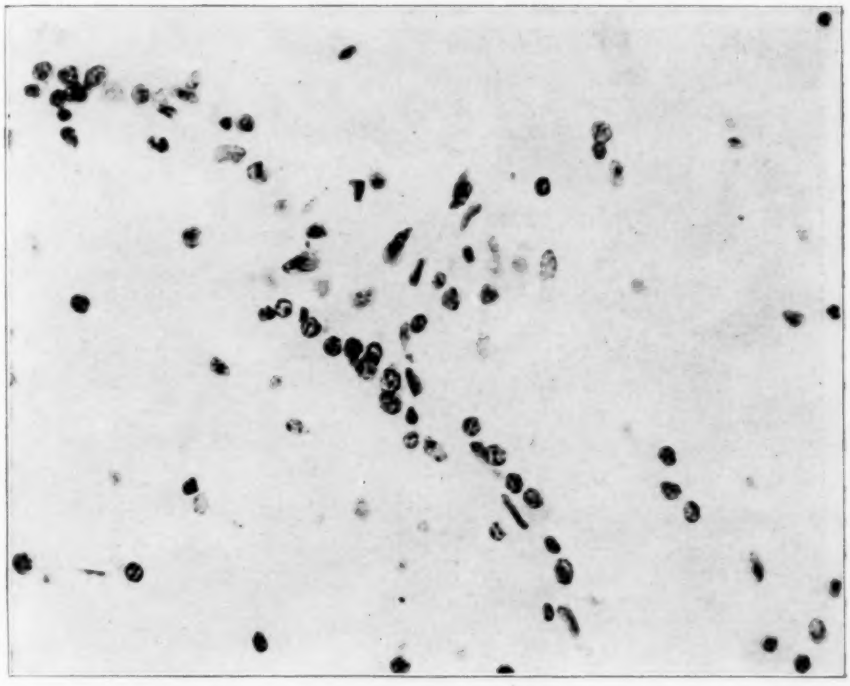

Fig. 6.—A higher power photomicrograph of the section shown in Figure 5. Details of the infiltrating cells, and a number of degenerating cells described in the text are shown.

SUMMARY AND COMMENT

Histopathologic study of the brains from three monkeys treated for a period of three months by intramuscular injection and inunction, respectively, of different mercurials, revealed a number of distinct tissue changes. These may be summarized as follows: (1) The pia-arachnoid was locally thickened and cellular; this was most pronounced in the sulci and was chiefly due to fibroblastic hyperplasia. (2) The endothelium of many capillaries and of the small vessels in general was large and swollen and in a state of active proliferation.

New vessel formation, as evidenced by capillary budding, was frequently observed. (3) A mild and nowhere striking infiltration of the adventitial lymph spaces of the smallest vessels with lymphocytes, plasma cells, and intermediate forms was present. (4) There was a moderate proliferation of the cellular as well as the fiber-forming neuroglia. The former was most distinct about proliferating capillaries, in the white matter and in the neighborhood of diseased ganglion cells; the latter was best seen in the subependymal and marginal cortical layers. (5) A relatively small number of ganglion cells were in a state of acute degeneration. (6) The distribution of the lesions mentioned was irregular, mainly local in character, and on the whole most pronounced in the basal portions of the brain.

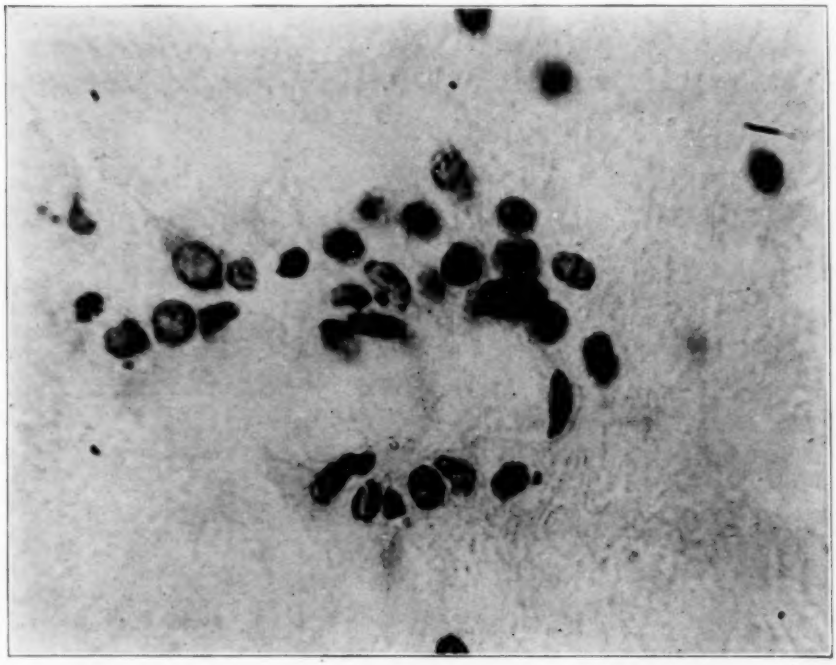

Fig. 7.—Centrum ovale of Monkey 1. A small vessel exhibiting greatly swollen endothelium and a few large round cells in the adventitial space.

The lesions described affect chiefly the capillaries and small vessels; they are proliferative, degenerative and mildly exudative in character; they, therefore, correspond to our conception of a reaction to an irritant. A comparison with the tissue alterations occurring in the central nervous system after intoxication with two other metallic poisons, lead and arsenic, discloses an essential similarity. The neuropathologic picture of arsenical poisoning has been described by Jacob, Weygand

and Kafka[4]; these observers injected solutions of arsphenamin and neo-arsphenamin into the central nervous system of monkeys. The changes of lead encephalopathy have been recently summarized by Hassin,[5] who confirms the results of similar studies by Mott[6] and Bonfiglio.[7] Hassin[5] showed that lead and arsenic induce nervous changes that may be designated as toxic nonsuppurative encephalitis, and he differentiated the changes produced by these metals from those characteristic of the infectious types of nonsuppurative encephalitis. As examples of the latter group, epidemic encephalitis and poliomyelitis may be mentioned; in these infections infiltrative and exudative phenomena characterize the picture, while proliferative alterations preponderate in the toxic group.

While we are in general accord with Hassin's statements, it seems to us, however, that the lesions of certain chronic infections (i. e., syphilis) are more difficult to separate from the infectious type mentioned above, for in syphilis proliferative changes are as prominent as, if not more prominent than, degeneration and exudation. In dementia paralytica, which is universally regarded as due to syphilis, the histopathologic picture consists essentially in new vessel formation, marked swelling of the vascular endothelium, infiltration of the adventitial spaces and the nervous parenchyma by certain round cells probably derived from the blood or lymph stream, the occurrence of rod (Stäbchen) cells, proliferation of the neuroglia of all types, and various degenerative changes of the ganglion cells and other structures. The lesions of general paralysis are most commonly confined to the frontocentral parts of the cerebral hemispheres, but cases occur in which other parts of the brain are more involved.

Now these changes of general paralysis are, in their essential nature, similar to those we have just described as resulting from experimental mercurial administration. In point of severity, however, the lesions due to mercury are far less intense.

While there can be no doubt that syphilis is the essential cause of general paralysis, it is still an open question whether other factors,

4. Jacob, A., Weygand, W., and Kafka, V.: Klinische und experimentelle Erfahrungen bei Salvarsaninjektionen in das Zentralnervensystem, München. med. Wchnschr. **61**:1608, 1914.

5. Hassin, G. B.: The Contrast Between the Brain Lesions Produced by Lead and Other Inorganic Poisons and Those Caused by Epidemic Encephalitis, Arch. Neurol. & Psychiat. **6**:268 (Sept.) 1921.

6. Mott, F. W.: Examination of the Nervous System in a Case of Chronic Lead Encephalitis, Arch. Neurol. & Psychiat., London, **4**:117, 1909.

7. Bonfiglio, F.: Circa le alterazioni della corteccia cerebrale conseguenti ad intossicazione sperimentale da carbonato di piombo (Encephalite produttiva), Nissl-Alzheimer's Arb. **3**:359, 1909.

among them mercury, arsenic, or other metals, may not play a subordinate rôle in the establishment of this entity. It must be distinctly understood, however, that no evidence has as yet been adduced that any of the clinical manifestations of general paralysis are due to mercury. We do not wish to be understood as putting forth the claim that mercury is responsible for the principal lesions of general paralysis, but, in view of our experimental results in monkeys, we feel justified in asserting that this metal and possibly other organic poisons may produce structural alterations of sufficient degree to influence the histopathologic picture. In this connection it is well to bear in mind that the salts of mercury (as well as those of arsenic and lead) produce tissue changes in many organs (kidneys, liver, gastro-intestinal tract, etc.), and that the mercurials in particular call forth distinct alterations in the blood-capillary system. It would be remarkable if the nervous tissue should be exempted. Added experiments are necessary and it is particularly desirable to study the influence on animals of mercurial treatment continued over longer periods of time, for, as Mallory[8] says, "It is impossible to produce in months lesions for which nature requires years."

CONCLUSIONS

1. Mercury, administered over a period of three months to monkeys, causes proliferative, degenerative, and slight exudative changes in the central nervous system.

2. It is suggested that mercurial administrations may play a minor rôle in the production of the histopathologic picture of general paralysis.

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8. Mallory, F. B., Parker, Frederic, Jr., and Nye, R. N.: Experimental Pigment Cirrhosis Due to Copper and Its Relation to Hemochromatosis, J. Med. Research, **42**:461, 1921.

SELLA TURCICA OF MONGOLIAN IMBECILES*

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From time to time the maldevelopment of the mongolian imbecile has been attributed to one gland or another. In 1916, Stevens [1] wrote "The characteristic facies of the mongolian syndrome and the dwarfing of the body make it probable that the syphilis acts primarily on some of the endocrine organs, possibly the pituitary body."

Later, Timme [2] described a peculiarity of the sella turcica which was present in twenty-three of his twenty-four cases. "This change consisted in an excavation under the anterior clinoid processes and presumably under the olivary process and the optic groove." He questioned whether or not it bore some relation to pituitary function.

Clift [3] thought this condition no more constant than in normals and pointed out a developmental deficiency of the nose and maxilla and generalized delay of bone development as the only characteristic roentgen-ray findings.

The data here reported were obtained with the view of testing these reports and with the purpose of determining what this "excavation" might mean. Radiograms were taken of thirty individuals comprising three groups: Group 1, consisting of ten unselected mongolian imbeciles; Group 2, of five mongolian imbeciles under twelve and five over twenty-seven; and Group 3, of five normals under twelve and five over twenty-two years of age. All were females. These radiograms were taken at a distance of thirty-six inches in order to insure less distortion.

From these radiograms, tracings of the sellae were made on celluloid and from this on paper. In order to eliminate as far as possible a personal error resulting from the necessity of choice of what to include in the tracing, the tracings were made independently by

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* From The Department of Medical Research, The Training School at Vineland, N. J., and the Department of Research, The State Home, Vineland, N. J.

1. Stevens, H. C.: The Cerebrospinal Fluid in Mongolian Idiocy, J. A. M. A. **66**:1373 (April 29) 1916.

2. Timme, Walter: The Mongolian Idiot, a Preliminary Note on the Sella Turcica Findings, Arch. Neurol. & Psychiat. **5**:568 (May) 1921.

3. Clift, M. W.: Roentgenological Findings in Mongolism, Am. J. Roentgenol. **9**:420 (July) 1922.

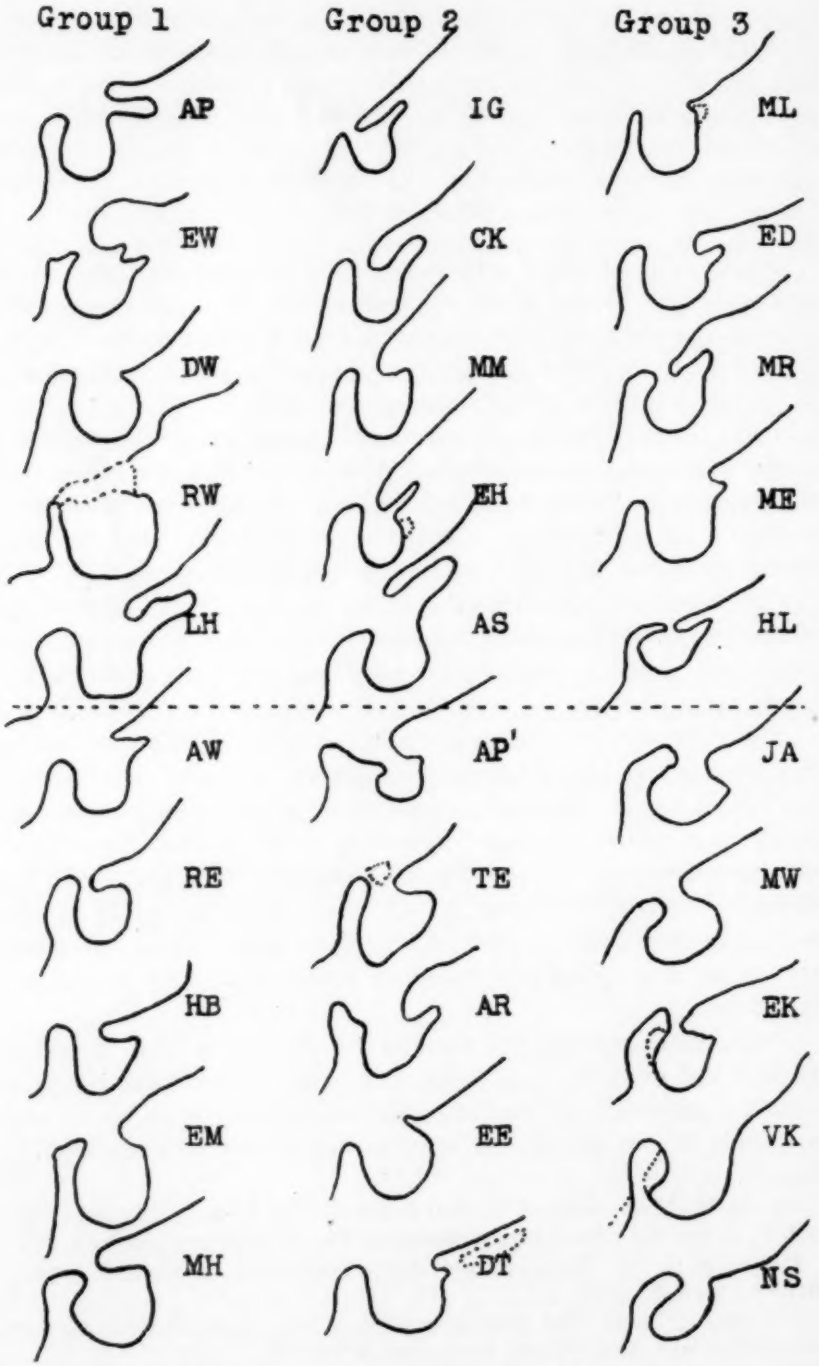

Fig. 1.—Tracings from roentgenograms of the sella turcica in mongolian imbeciles and normals.

two of us. All but nine of these duplicate tracings agreed well and of these nine, five were decided by again tracing the plates. The remaining four were decided by repeating the radiograms one or more times. When there was any doubt about the position of a line a dotted alternate line was made.

These tracings (Fig. 1) correspond according to columns with the groups chosen. The accompanying table is the key to the ages and rank order of prominence of the "excavation" in Figure 1 and corresponds with this figure in the positions of the individuals. In determining the rank order of the various tracings, all possibility of bias was eliminated by tracing the sellae separately on small pieces of paper and submitting these to three individuals unacquainted with the problem. Case AS was given as an example of the character to be rated. All three judges selected the same first fourteen and one

Ranking of "Excavation" in Radiograms

Group 1 Mongolians			Group 2 Mongolians			Group 3 Controls		
Name	Age	Rank	Name	Age	Rank	Name	Age	Rank
AP	12	4	IG	6	6	ML	11	
EW	15	13	CK	9	3	ED	10	11
DW	16		MM	11		MR	11	7
RW	17		EH	12	5	ME	10	14
LH	18	2	AS	12	1	HL	11	8
AW	18	10	AP'	27	15	JA	23	
RE	20		PE	27		MW		
HB	20	12	AR	27	9	EK	22	
EM	23		EE	28		VK	24	
MH	25		DT	33		NS	26	

of them selected DT for the fifteenth. Thus there was good general agreement on the rating. The remaining fifteen varied so little among themselves as to the excavation, that for comparison of intensity a distribution of fifteen points would not have given the true relation to the first fifteen. These were therefore not rated.

Group 1, selected at the beginning of the investigation, showed a prominence of the "excavations" among the younger individuals. That is, the five persons who showed it most prominently averaged over three years younger than the five who showed it least prominently. Thus Group 2, with Group 3 as a control, were chosen. In order to study the characteristics under question, radiograms were taken of a skull (Fig. 2). This was the skull of an unknown individual and was taken from a regular articulated skeleton such as is used for demonstration purposes. The age and shape of the cranium were against its being a mongolian. According to the above rating of the intensity of the "excavation," that of this skull was placed between third and fourth.

RESULTS

Inspection of the table shows at once the preponderance of cases above the line, separating the younger from the older cases. Only four of fifteen appear below the line and, of these, two were eighteen and twenty years of age respectively. It is further seen that all up to the ninth in order are in the younger group.

It is seen that the "excavation" is on the average about twice as prominent in children of Group 2 as in children of Group 3, and that, while the adult controls contain none of the first fifteen, the adult mongolians contain two.

Inspection of the radiogram of the skull shows that it possesses a most clearly outlined narrow "excavation." Had all of the soft parts been present as in the living head this might not have been seen.

Fig. 2.—Roentgenogram of sella turcica from a dried skull.

Inspection of the skull shows no excavation under the olivary process or optic grooves. The "excavation" corresponds well with the decrease of the bone to be penetrated as the rays pass inferior to the anterior clinoids through the optic foramen and superior to the olivary process. Slightly above this level they must pass through both clinoids whereas slightly below they must pass through the olivary process.

CONCLUSIONS

From the observations detailed, it may be concluded that the so-called "excavation" is present in childhood and usually disappears with development toward maturity. Its greater pronouncedness in mongolians is probably a corollary of the peculiar facial architecture and of the generalized delay of bone development announced by Clift.

Its significance is best understood when we realize that there is a constant, slow reorganization of bony relations up to the completion of ossification; that the sphenoid is especially a slowly ossifying bone, not reaching completion until about the twenty-fifth year; and that the particular area in question "under the olivary process" begins to be hollowed out for the formation of sphenoid sinuses only at the eighth year, continuing this process for years subsequently. Thus an interpretation of the findings in the olivary process must be very carefully controlled, age for age. From study of the radiogram of the skull, it is probable that the "excavation" is dependent for its presence and its size on differences in the levels of the anterior clinoid processes and the olivary processes and that consequently its contents would be the optic nerves and chiasma and the ophthalmic arteries.

A CASE OF PORENCEPHALIC DEFECT ASSOCIATED WITH TUBERCULOUS ENCEPHALITIS

A HISTOPATHOLOGIC SUPPORT TO THE STRÜMPELL THEORY OF INFLAMMATION

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Porencephalus was first so termed by Heschl,[1] in 1859, in his description of brain defects characterized by cavity formations. There still exists considerable doubt as to the primary lesion or cause of these defects, which are often represented by large areas or spaces in the cerebral substance filled with cerebrospinal fluid and covered by pia mater. Heschl, who drew his deductions from gross anatomic studies, considered the loss of brain substance to be due to faulty development from an intra-uterine injury to the anlages of the brain parts. Later,[2] he admitted the possibility that regressive vascular changes, and perhaps also syphilis, are instrumental in producing the defect. Strümpell [3] held that it was due to some type of encephalitis of the gray matter, probably analgous to anterior poliomyelitis, a view supported by Schultze [4]; and Limbeck [5] published a study of four cases that tended to support the inflammatory origin. It is generally considered, however, that Strümpell's theory is not proved, though a recent histopathologic study by Globus [6] has added another case to the Strümpell group.

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1. Heschl: Gehirndefekt und Hydrocephalus, Prag. Vrtljhrschrf. prakt. Heilk **61**: 1859.

2. Heschl: Neue Fälle von Porencephalie, Jubelaeums Band der Prag. Vrtljhrschr. **100**:40, 1868.

3. Strümpell: Ueber die Akute Encephalitis der Kinder, Jahrb. f. Kinderh. **22**: 1884.

4. Schultze, F.: Beitrag zur Lehre von den Angebornen Hirndefekten (Porencephalie), 58 Versammlung Deutscher Naturforscher und Aerzte in Strassburg, 1885.

5. Limbeck: Zur Kentniss der Encephalitis congenita in ihrer Beziehung zur Porencephalie, Ztschr. f. Heilk **7**: 1886.

6. Globus, J. H.: A Contribution to the Histopathology of Porencephalus, Arch. Neurol. & Psychiat. **6**:652 (Dec.) 1921.

Among the possible causes for porencephalus, Kundrat [7] emphasized (*a*) local thrombosis of cerebral vessels, (*b*) intra-uterine cerebral hemorrhages, and (*c*) interference with the fetal circulation. Wigglesworth [8] stated: "A destructive encephalitis occurring during fetal life or early infancy would no doubt explain the appearances presented, although it might be difficult to understand how such a process could be started. I am rather inclined to the idea that the lesion is the result of injury inflicted during the process of birth not improbably by means of the forceps."

In view of the small number of cases of porencephalus associated with progressive inflammatory lesions which have been thoroughly studied microscopically and recorded in the literature, we wish to present a case in which the lesion was tuberculous in character, thus serving as a contribution to the infectious, inflammatory conception of the origin of the defect.

REPORT OF A CASE

Clinical History.—I. Jr., a colored boy, aged 4, was admitted to the Crownsville State Hospital, July 10, 1920, having been transferred from St. Elizabeth's Home, Maryland, to which he had been committed at the age of 3 by an order of the Juvenile Court.

The father, aged 51, is the only survivor of eleven children, all others having died in infancy. He appeared healthy and stated that his only illness was pleurisy two years ago. He refused a physical examination for tuberculosis. The mother, aged 40, had been sent to the Industrial Home for Colored Girls at age 14, from which, after a short time, she was paroled as domestic in a private family. At this period she was said to be eccentric and given to violent outbreaks of temper, followed by periods of depression. She had twelve children and one miscarriage. In January, 1918, when she went to a hospital for surgical treatment, she gave a history of coughing attacks with spitting of blood for two weeks; the blood Wassermann reaction was negative. In May, 1922, no evidence of tuberculosis was found at the University Tuberculosis Clinic. A brother, J., aged 14, is said to have been subject to fits, the character of which is not known. A sister E, aged 18, was committed to the Industrial School for girls at Melvale in January, 1921, where she still resides. Mentally she is very dull, but not troublesome. She has never menstruated, which fact taken with her physical build suggests defect in endocrine development. Another sister L, aged 11, was committed to St. Elizabeth's Home by the Circuit Court with a history of being incorrigible, fearful at night, and greatly retarded mentally. Sister A, aged 12, was committed to the Industrial School at Melvale in January, 1922, where she gave a great deal of trouble, was rude, wild and considered to be low grade mentally. No definite history of the other children was available.

No history of the patient was obtained until he was committed to St. Elizabeth's Home, Maryland, at the age of three. He was then unable to use either arms or legs and took no notice of his surroundings. After four months his attention could be attracted and he seemed momentarily to dis-

7. Kundrat: Die Porencephalie, Eine anatomische Studie, Gratz, 1882.
8. Wigglesworth: Brain **20**: Parts 77-78, 1897.

tinguish persons. After six months he began to pick up articles such as spoons and toys, but did not hold them for any length of time. He tried to build with blocks, but, failing repeatedly, would stare about with an unintelligent facial expression. After nine months, he astonished those in charge by making an attempt to talk, and after twelve months he was able to commit to memory very short sentences, which were retained for the day only. At this time he was unable to move his extremities and had to be carried everywhere. On admission to the Crownsville State Hospital at the age of 4, his behavior was quiet and listless, he apparently took no notice of his surroundings and was completely helpless.

Behavior.—At first his attention could be attracted with great difficulty by snapping the fingers or lighting a match, but was only momentarily held. He seemed to recognize the attending physicians and nurses and had been taught to make an effort to call the attendants by rapping on the bed when he wanted to go to the toilet. He was very untidy and was destructive to clothes and furniture in his feeble way. He was generally cheerful and played with blocks by shuffling them over the floor without any attempt to construct anything with them. Frequent attempts were made to teach him to repeat letters and figures, but without response. Grinding of the teeth, a silly grin, and an anxious facial expression were constantly alternating symptoms.

Physical Examination.—Weight 40 pounds (18 kg.), height 26 inches (66 cm.). The skull was dolichocephalic in type and there was a slight bulging, about the size of a small orange, over the left parietal area. The fontanels were patent and the sagittal suture was open and separating. The nose was typical of the race, and the ears were quite small and contracted, the lobules adherent to and confluent with the skin of the face. The palate was very narrow and high. There was a convergent strabismus, but the pupils were regular, equal and reacted normally. He did not use the right arm and leg, which were about half the size of the opposite extremities; the right leg was flexed (contractured) at the knee to an angle of 40 degrees; the right arm was spastic, flexed to about 40 degrees at the elbow and he was unable to hold objects in the hand, the fingers of which were flaccid and powerless. The left arm was slightly contracted (flexed at the elbow), but he had some use of this hand, being able to feed himself; he had been seen attempting to peel an orange by holding it between his knees and using the fingers of the left hand. He also had some use of the left leg. There was a left dorsal curvature of the spine. If placed in a standing position he was unable to sustain himself by holding to a support with the left hand but, if not held, would fall to the floor. With the use of the left arm, he would shuffle over the floor on the left hip which was heavily calloused from this crawling.

The skin was dry and scaly, the muscles poorly developed and undernourished and the superficial cervical lymph glands were indurated. The clavicular spaces were depressed, the shoulders drooped and thoracic expansion was poor. Examination of the circulatory system gave negative results. The lung expansion was poor and delayed bilaterally, and the percussion note was impaired over the entire left lung. The breath sounds were high pitched and there was diminished vocal resonance on both sides. The spleen and liver were enlarged and there was a small umbilical hernia. The abdomen was scaphoid in shape.

The right patellar reflex was absent, but the left was exaggerated and there was a Babinski sign on the left side. Other deep and superficial reflexes

were normal. Sensation was absent over the entire right side (face, arm, trunk and leg); the skin of the left side was markedly hyperesthetic.

Progress.—The condition remained practically stationary until three months before death, when gradual failure was noticed, with rapid loss of weight, increased untidiness with both urine and feces, and retention of a posture in which he was placed for hours if he was not disturbed. He was confined to bed, and did not use arms or legs for three weeks before death. He refused food, and fretted constantly; he lay on his left side with the body slightly bowed. The temperature varied between 100 and 101 F., with a slight evening rise; the pulse ranged between 110 and 120.

Necropsy.—The musculature was poorly developed, emaciated, soft and flabby, with contracture of both legs at the knees; the entire right side of the body was either arrested in growth or atrophied, since it was about one-half the size of the left. There was a moderate left dorsal curvature. The heart and blood vessels were negative with the exceptions that the walls of the right pulmonary vessels were thickened and inelastic, and the portal vein was unusually thick and rigid.

The thoracic cavities were free from fluid, and the organs were in normal position. The left lung was free, and the pleura normal, but the substance was markedly congested, with some red hepatization, and was filled with miliary tubercles. The pleura of the right lung was deeply infiltrated and presented adhesions at the apex posteriorly and around the hilus. The lung substance was firm and exhibited many miliary and conglomerate tubercles; the invasion began at the hilus and traversed both upper and lower lobes. Some of the tuberculous nodules were the size of nutmegs. The bronchioles were greatly thickened and surrounded by infiltrated zones.

The peritoneum, stomach and intestines were not remarkable. The bile passages were thickened and deeply stained. The mesenteries were heavily infiltrated, and the mesenteric lymph nodes were tuberculous. The liver was congested and exhibited tubercles of large size throughout the substance; the spleen was congested and filled with large tubercles. The pancreas was moderately congested but presented no tubercles although the adjacent lymph nodes were involved. The thymus was small and regressive in type, and there were no gross abnormalities in the pituitary, thyroid and adrenals.

The brain weighed 645 gm. and the surface showed a chronic leptomeningitis with a thickened, adherent pia mater. The posterior half of the left hemisphere was bulging with fluid content and collapsed on rupture of the transparent wall; the remnant of the other atrophied brain substance is illustrated by the shaded area in Figure 1. A large amount of clear cerebrospinal fluid came from this cavity which was an extension of the posterior lateral wall of the greatly dilated left lateral ventricle. The right lateral ventricle was also markedly dilated, being filled with fluid which exerted pressure on all surrounding wall structures.

The porencephalic defect was complete, with obliteration or complete atrophy of the entire brain substance of the following structures of the left hemisphere: (1) Greater portion of the middle one-third of the gyrus centralis posterior, (2) gyrus supramarginalis, (3) gyrus angularis, (4) lower one-half of the lobulus parietalis superior, (5) posterior one-fourth of the gyrus temporalis superior, (6) posterior one-fourth of the gyrus temporalis medius, and (7) anterior one-half of the gyri occipitalis transversales. Surrounding this defect there was a wide zone of atrophied brain substance, the atrophy becoming progressively less as the borders of the hemisphere were approached (in

Fig. 1 A, the stippled area denotes marked atrophy of both cortex and white substance), but there were no normal convolutions, all showing pressure atrophy in some degree.

The surface of the right hemisphere exhibited irritative and pressure changes; previous to removal of the pia there was no evidence of tuberculosis, but on stripping this and sectioning the brain, the following areas of active tuberculous encephalitis with central caseation and surrounding inflammatory reactions were revealed: (1) Right gyrus frontalis superior, length 3 cm., diameter 1 cm. (Fig. 1 B); (2) right occipital lobe, 2 by 2 cm. (Fig. 1, B and

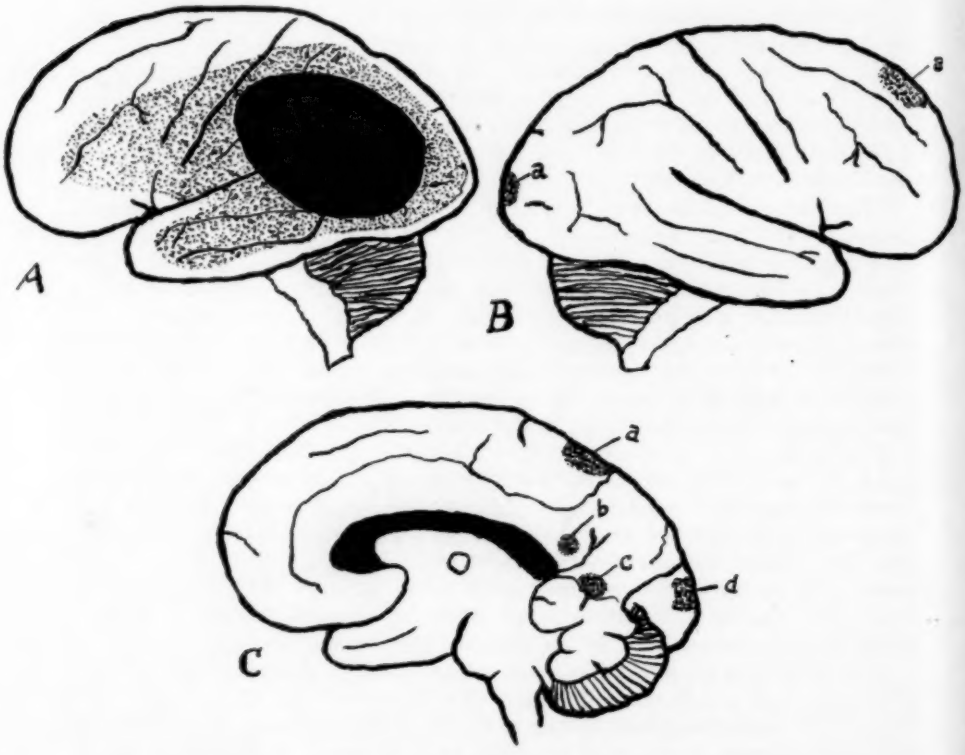

Fig. 1.—A. Sketch of left hemisphere showing area (block) of complete absence of brain tissue and surrounding area (stippled) of advanced convolutional atrophy with obliteration of fissures.

B. Right hemisphere showing areas (a, a) of active tuberculous encephalitis.

C. Mesial surface of right hemisphere showing areas (a, b, c, d) of active tuberculous encephalitis.

C); (3) two round areas about 1 cm. in diameter, one on each side of the sulcus subparietalis (Fig. 1 C, b and c) of the mesial surface of the right hemisphere; and (4) a round active tuberculous area 1 cm. in diameter in the center of the right thalamus (Fig. 2). Careful sectioning of the brain substance failed to disclose other areas of active tuberculous encephalitis.

HISTOPATHOLOGIC EXAMINATION

1. *Areas of Active Tuberculosis.*—(1) Occipital Lobe.—There was a wide central zone of dense caseation necrosis, in some areas of which the outlines of mononuclear cells were still visible. The margins of the caseated area were irregular and indented by masses of densely packed lymphocytes, endothelial cells, gitter cells and strands of fibrin. An outer zone characterized by many small blood vessels surrounded by endothelial cells, plasma cells and small lymphocytes, as well as diffuse exudate, gradually faded out into more normal but edematous brain structure. In patches the phagocytic cells were very large, filled with fat, and presented two or three nuclei; often they bore bizarre nuclear shapes. These areas of inflammation were apparently rather rapidly extending and showed very little evidence of a successful healing reaction. The adjacent neuron cells were badly damaged and showed secondary degenerative changes.

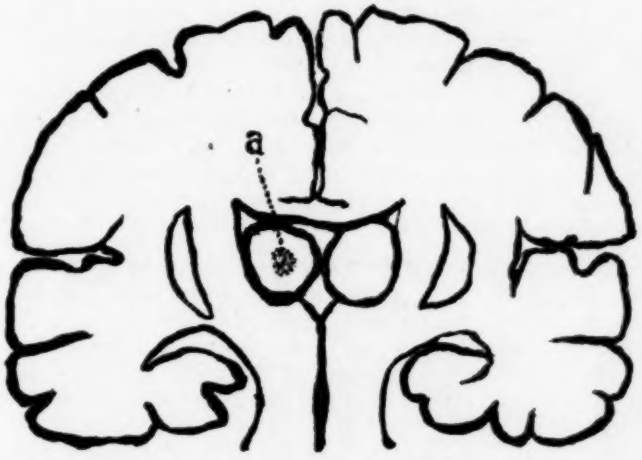

Fig. 2.—Area of active tuberculous encephalitis in the center of the right optic thalamus.

(2) Frontal Area.—These sections were attached to meninges in the meshes of which there were large accumulations of pink stained fluid, and a moderate infiltration of the usual types of mononuclear cells many of which were plasma cells. The meninges showed no tubercles over the surfaces of the convolutions, but the meningeal extensions into the fissures were accompanied by dense lymphocyte infiltration, and terminated in large tuberculous caseations in the deeper brain substance. There was an occasional, small tubercle in the walls of the meningeal vessels in the fissures.

The large area of tuberculosis was composed of multiple caseations separated by zones of dense accumulations of the mononuclear cells mentioned above. There were many new formed blood vessels and marginal fibroblastic productions. Small patches of lymphocytes and endothelial types were seen far out in the brain structure, where many vessels also exhibited perivascular lymph space infiltration. The brain tissue near these areas, which included both cortex and white matter, was very edematous. Occasionally the perivascular spaces were widely dilated and filled with an acellular, homogeneous fluid. Large

accumulations of this fluid were seen in pockets about the tubercles quite apart from the blood vessel spaces.

(3) Optic Thalamus.—These sections disclosed practically the same reaction described for the other tuberculous areas, but the zone of round cell infiltration and cellular reaction was much narrower and there was a greater tendency to fibroblast production and healing. There was considerable edema throughout and the thalamic neuron cells showed advanced secondary degenerations and varicosed dendrites.

Special staining methods demonstrated the presence of tubercle bacilli in sections from several of the areas described.

2. *Completely Atrophied Regions.*—The brain tissue was absent over a large gap which was covered by a membrane of wavy dense fibrous tissue in which fibroblasts and small lymphocytes were noted in linear formations. This picture gradually changed toward the periphery of the aplastic area.

3. *Partially Atrophied Regions.*—(1) The pia mater could be differentiated from the upper layer of the cortex. The pia mater in general was thick, dense and fibrous with numerous attachments, distinct neuroglial bridgings, and focal fusions with the upper layers of the cortex. The vessels were moderately thickened and some were surrounded by a thick cellular exudate composed chiefly of lymphocytes and endothelial cells. Near some of the short fissures this mononuclear exudate became more diffuse and followed the extensions deeply into the crevices. Frequently, in the shallow fissures the healing process was in command and fibrous tissue with neuroglial scar productions had replaced the active exudate.

(2) The adjacent narrow cortex was not divisible into the classical cortical cell layers. The neuron cells were few in number, small, irregular in outline and reacted strongly to the basic stains, the Nissl bodies being invisible and the nucleoli frequently absent. In the central and lower cortical areas there was only a moderate overgrowth of neuroglia, but near the meninges there were large dense patches of these cells extending to the surface and blending with the pia mater.

(3) Sections of the white matter exhibited much degeneration of fibers and great condensation from pressure. There was no exudate about the vessels of this substance but there was a general overgrowth of neuroglia. This area of white fibers gradually shaded out into a pale zone which was wider than, but apparently represented, the subependymal tissue, since it was nearest the dilated ventricle. There were no signs of ependymal lining cells, but the margin was composed of dense neuroglial and chronic inflammatory cell formations. The zone of tissue nearest the ventricle was literally filled with an exudate of lymphocytes, plasma cells and endothelial leukocytes with an abundance of neuroglia cells. The exudate was particularly dense and accentuated about all blood vessels. No focal tuberculous formations were noted.

(4) The brain tissue, which could be divided into three zones (cortex, white matter, and lower inflammatory zone), became wider and progressively less affected the greater the distance from the completely aplastic area, but in all sections the zone next the ventricle still exhibited both a diffuse and a perivascular exudate although signs of healing were more pronounced. Several sections from different areas of cortex distant from the principal lesion were examined and found to be covered by a thickened pia mater on which were numerous patches of endothelial cell overgrowth and in some instances a monocellular pial exudate extended into the fissures. No tubercles were

seen in the pia either about the surface vessels or in the depths of the fissures. Neuroglial felting was present in various degrees in the marginal layers of the cortex of the sections remote from the principal lesions. In general, the cortex was rather dense with increased neuroglia and the neuron cells were small, undeveloped and deranged. The blood vessels were universally slightly thickened and an occasional ruptured capillary was seen.

4. *Lenticular Nuclei.*—The ependymal covering was completely replaced by densely felted neuroglia cells among which endothelial leukocytes were scattered. There was a dense perivascular exudate, and frequently, in addition, there were recent ruptures in the vessel walls, with free hemorrhages into the tissues. The perivascular exudates of these sections were composed chiefly of small lymphocytes which reacted strongly to the stains. No tubercles were seen. The deeper structures were dense with neuroglial production and all blood vessels were thickened and distorted, although there was no perivascular exudate. There were advanced degenerative changes in many of the neuron cells and also much degeneration in the white fiber areas.

5. *Ependyma and Subependymal Tissues.*—Some of these sections contain all structures from the pia mater to the ependymal layer, the tissues showing great compression, cellular and fiber degeneration, with obliteration and a marked alteration in the general architecture. Normal ependymal cells were not seen, but a marginal neurogliosis, was the chief characteristic of this area. The several types of neuroglia were very numerous.

In some areas where the meninges, entire cortex, white matter and ependyma could be brought within a single field of the microscope, the blood vessels exhibited thromboses and a dense lymphogenous perivascular exudate; only traces of the white fibers and residuals of the cortical nerve cells remained, while the ependymal elements were entirely replaced by neuroglia. No active tuberculous granulation tissue was present in these strips.

6. *Cortex of Right Temporal Lobe.*—The pia mater covering the cortex was infiltrated with lymphocytes, contained many fibroblastic productions and was attached to the underlying cortex by very extensive neuroglial and fibrous bridgings. The arachnoid spaces were largely obliterated and the vessels of both meninges and cortex were thickened and markedly congested, but those of the cortex were not surrounded by exudate. Many neuron cells of the cortex showed arrest in growth, were pale and exhibited very small nuclei; other cells were in stages of secondary degeneration; and still others were altered by prolonged pressure factors.

7. *Aqueduct of Sylvius.*—The surface structures of the corpora quadrigemina exhibited a mild perivascular exudate as well as some diffuse exudate of lymphocytes and endothelial leukocytes. Many distorted structures from pressure changes were encountered, and the neuroglial overgrowth was abundant throughout. The aqueduct was collapsed and surrounded by proliferating neuroglia cells and exudate which was principally about the small vessels. The nerve cells were swollen and weakly stained, and many showed secondary pigmentations.

8. *Pons and Medulla.*—Along the left margin of the pons, there were a few vessels showing a perivascular exudate which gradually fused with the substance involving some of the pons nuclei where many parenchymatous cells had been destroyed. The pons nuclei not involved by the exudate were swollen and exhibited acute cloudy changes, as did also the parenchymatous cells of the medulla. No exudate was discovered in the medulla; apparently this

structure had escaped the primary, but not the secondary, effects of the tuberculous irritation.

9. *Cerebellum.*—There was no apparent neuroglial over-production in the cerebellum and with the exception of the overlying pia mater the organ appeared normal microscopically. In general the pia was thickened by fibroblasts and was infiltrated by an unusually large number of endothelial leukocytes and plasma cells. In patches there were also some small lymphocytes which were limited to the surface. Deep in the fissures there was practically no exudate excepting around some of the larger vessels.

10. *Meninges of Spinal Cord Containing Peripheral Nerve Bundles.*—In the meninges there was a large amount of exudate composed of endothelial leukocytes, plasma cells, gitter cells, small lymphocytes, red blood corpuscles and fibrin, with the small lymphocytes predominating. The blood vessels were surrounded by tuberculous granulation tissue. There were numerous degenerations in the myelin sheaths of the peripheral nerves, and in places the nerve had undergone complete sclerosis. The perineurium and epineurium were both universally and heavily infiltrated with small lymphocytes.

11. *Cervical Cord.*—The parenchymatous cells of the anterior horns were fairly well preserved, but a few showed secondary swelling. The gray matter in general was quite edematous and presented also a universal perivascular exudate of small lymphocytes. The dura mater surrounding the cord was heavily infiltrated by tuberculous exudate and the pia-arachnoid was filled with tuberculous granulation tissue, which had developed in the vessel walls and extended along the sheaths of the peripheral nerves. This exudate entirely surrounded the cord and had infiltrated its structures, including the fissures, pial extensions and marginal vessels.

The remainder of the spinal cord was not removed from the body, and the lower levels were not available for comparative study.

COMMENTS

In this case active tuberculous encephalitis, with the bacilli demonstrable in the tissues, and the usual lymphocyte, endothelial cell and fibrin reactions, was present in the occipital, frontal, parietal and thalamic areas; however, there was no general involvement of the meninges, but an occasional tubercle was encountered in the walls of vessels in the pia-arachnoid of the fissures.

In some areas of the cortex there were fissures filled with active monocellular meningeal exudate, with some superficial extension of the process into the brain substance; while, in other cortical zones, this active process had once obtained, but had been overcome by the reconstructive forces so that healing by neuroglial productions and fibroblasts was the predominating reaction. In many places, both on the surface of the convolutions and in the sulci, the arachnoid spaces had been obliterated by tangles of neuroglial cells and fibroblasts.

Evidence, both of active acute exudate and of various stages of healing, was found in the subependymal substance of the lateral ventricles and also in the structures about the aqueduct of Sylvius. Through all areas examined microscopically, the neuron elements showed pro-

found secondary degenerations, but this change was most pronounced in the zones near the actual defect where meninges, cortex and white matter were fused and could be differentiated only with great difficulty.

There were sufficient gross and microscopic changes in the brain to account for the neurologic symptoms during life, and, while active tuberculosis was not encountered at the margins of the porencephalic defect, there were signs of former inflammatory processes adequate as evidence to show the results of an early encephalitis. It was impossible to determine positively whether the porencephalic defect was due to a healed tuberculous focus or was caused by an invasion with some other pathogenic organism; however, since there were patches of both active and healed tuberculosis in other brain areas, it is supposed by the authors that the defect was the original focus of tuberculosis in the brain.

Since there were no definite findings indicative of tuberculosis in the mother, there is some question as to whether the destructive process started in late intra-uterine life from general infection of the fetus or was the result of tuberculosis acquired in childhood. According to Whitman and Greene,[9] congenital or intra-uterine tuberculosis is extremely rare, but they and others[10] have proved its occurrence by finding the lesions in the still-born fetus.

After analyzing a case, Seeligmüller[11] conceived that latent tuberculosis was almost the sole cause of infantile hemiplegia; however, we feel that our case serves only as an additional argument in favor of the infectious, inflammatory etiology of some porencephalic defects, with or without hemiplegia.[12]

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9. Whitman, R. C., and Greene, L. W.: Case of Disseminated Miliary Tuberculosis in a Still Born Fetus, Arch. Int. Med. **29**:261 (Feb.) 1922.

10. Pratt, G. P.: Congenital Tuberculosis with Report of Case, Am. J. Dis. Child. **23**:88 (Jan.) 1922.

11. Seeligmüller: Jahrb. für. Kinderheilk. **13**: 1879.

12. In addition to the references already given, the following will be found of interest:

Virchow, Rudolph: Congenitale Encephalitis und Myelitis, Virchows Arch. f. path. Anat. **38**:129, 1867.

Sachs and Peterson: A Study of Cerebral Palsies of Early Life Based upon an Analysis of One Hundred and Forty Cases, J. Nerv. & Ment. Dis. **17**:319, 1890.

Clinch, T. A.: A Case of Imperfect Porencephaly, J. Ment. Sc. (April) 1899.

Norman, C., and Frazier, A.: A Case of Porencephaly, J. Ment. Sc. (Oct.) 1894.

Osler, William: The Cerebral Palsies of Children, Philadelphia, 1889.

Bianchi: Defetto porencephalico, La Psichiatria, Naples, 1884.

Audry: Les porencéphalies, Révue de méd. (June-July) 1888.

Kennard, K. S.: Case Report—Primary Tumor of Heart—Porencephalus, New York S. J. Med. **21**:346 (Sept.) 1921.

EXPERIMENTAL VESTIBULAR TREMORS, WITH ANALOGOUS CLINICAL CASES*

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Since the memorable work of Flourens in 1824, experiments on pigeons have contributed greatly to our knowledge of the anatomy and physiology of the static labyrinth. During the epidemic of 1918 and 1919, I treated a number of cases of epidemic cerebrospinal meningitis, in some of which postmeningitic vestibular symptoms were noted. Since my observations did not seem to be explained by the generally accepted views concerning the physiology of the membranous labyrinth, I have approached the problem experimentally during the past year and a half. In this work I have noted, not only the coarse "head nystagmus" and eye nystagmus found by so many investigators, but also a fine tremor which I have designated "vestibular tremor."

It will suffice for the scope of this paper if I call attention to the anatomic landmarks of the vestibular apparatus, the saccule, the utricle, and the three semicircular canals, the tubulated enlargements near the proximal extremities of which are known as ampullae and contain the nerve endings of the vestibular nerve. The anterior and posterior vertical canals meet at their distal extremities and are joined within a short space by the distal extremity of the horizontal canal, forming a common canal to the utricle. Herrick's modification of Ewald's diagram [1] shows the position of the semicircular canals. He says: "The anterior canal of one side lies in a plane parallel to that of the posterior canal of the other side."

One prevailing theory of the physiology is that within the confines of the membranous labyrinth a fluid, the endolymph, is contained, and that this fluid circulates, thereby acting as a stimulus to the vestibular nerve endings in saccule, utricle and ampulla. As yet I am not convinced that this theory is correct. I have shown [2] that, in the blind

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1. Herrick, C. J.: An Introduction to Neurology, Philadelphia: W. B. Saunders & Co., 1921, p. 202.

2. Woolsey, C. L.: Arch. Neurol. & Psychiat. **7**:526 (April) 1922.

pigeon, one-quarter of a rotation is sufficient to produce an after-nystagmus of two seconds duration. Then, if the pigeon is immediately rotated in the opposite direction, an opposite after-nystagmus is produced. The lumen of the canals being very small and more or less tortuous, it seems improbable that circulation of lymph could take place from such slight movement, and produce vestibular impulses. After a comprehensive study of the relations of the vertical canals, Jones,[3] states ". . . these two vertical canals act together. We know this for the following reasons: (1) They are both in the vertical axis, so that any movement in a vertical axis influences both. Experimentally, either douching with the head upright, or turning with the head forward or backward, affects both these canals. (2) Anatomically, at their innermost point, they unite in a common crus. The movement, therefore, of the endolymph in one canal cannot take place without a corresponding movement of the endolymph in the other." Since the horizontal canal joins the common canal not more than 1.5 mm. below the meeting point of the vertical canals, and since the horizontal canal and superior vertical canal have one meatus in common, the question arises: "Does not the lymph also flow in the horizontal canal when a lymph movement is under way in the superior vertical canal, providing lymph circulation is a fact?"

When the head is 60 degrees forward, none of the canals is horizontal; and when the head is 90 degrees backward, the anterior-superior canal is in the horizontal plane, and the posterior-vertical and horizontal canals are in vertical planes—although at right angles. Hence, in both instances, if cold douching is applied, the lymph in both these canals should gravitate downward. Applying Jones' theory of "movement in both verticals," it would seem that there must necessarily be a movement in all canals.

The rotation tests of Bárány are of interest in this connection. Anatomists,[1, 4] have shown that the anterior vertical canal of one side lies in a plane parallel to the plane of the posterior vertical canal of the contralateral side. Consequently, if either of these canals is put in a horizontal plane, the other must be in a horizontal plane. If rotation is then performed, both canals are affected. That is, there should be movement of endolymph in both; and, if Jones' theory is correct, that movement of the lymph in one vertical produces movement in the other, then the rotation tests I have described above should cause movement of the endolymph in all the vertical canals.

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3. Jones, I. H.: Equilibrium and Vertigo, Philadelphia: J. B. Lippincott Co., 1918, p. 147.

4. Gray's Anatomy, Philadelphia: Lea & Febiger, 1918, p. 1052.

Many investigators, Goltz,[5] Mach,[6] Breuer,[7] Ewald,[8] and Gruenberg,[9] have opened the canals of pigeons and their observations, while not identical in all respects, quite agree that there is a "head movement" following such operative procedures. They agree that these movements persist for a few days. Stirling,[10] removed contralateral canals in dogs and produced "pendulum movements" of the head, which died out in from four to five days. He does not mention having observed the small "vestibular tremor" of which I have spoken. Most of his animals died in from ten to twenty days.

EXPERIMENTAL OBSERVATIONS

In performing the rotation test I have utilized an apparatus constructed from a small phonograph. The spring is removed and the spring barrels are bolted together so that the table may be rotated in either direction, one revolution of the crank producing 20 rotations of the disk. An aluminum disk, 14 inches in diameter, is fastened to the original disk. A U-shaped cradle of brass with holes in the sides is provided to hold the pigeon. The cradle is bolted to the aluminum disk; the pigeon is then placed in a cloth sack, with only head and neck exposed, and is fastened in the cradle by pulling parts of the sack through the holes and inserting safety-pins. A device for holding the head consists of an adjustable muzzle, into which the bill is thrust and retained by small leather or gauze head straps. It is thus possible to secure any position of the head desired. During operations, ether is administered through the muzzle.

The instruments used in canal operations I have constructed from discarded dental instruments. Great care must be taken in these operations on account of the blood vessels along the course of each canal. Bone wax is used to stop the hemorrhage. After a canal is opened, a small, annealed copper wire, or a horse hair is pushed into the canal down to the ampulla. By this method I know the extent of the damage produced; such methods as injecting alcohol into the canals must be condemned, since the extent of its penetration is not known.

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5. Goltz, F.: Ueber die physiologische Bedeutung der Bogengänge des Ohrlabyrinths, Pflüger's Archiv. **3**:172, 1870.

6. Mach, E.: Grundlinien der Lehre von den Bewegungsempfindungen, Leipsic, 1875.

7. Breuer, J.: Ueber die Funktion der Bogengänge des Ohrlabyrinths, Med. Jahrb., 1874, page 72.

8. Ewald, E.: Centralbl. f. d. med. Wissensch. **28**:114, 1890.

9. Gruenberg: Compensatory motions and the semicircular canals, J. Exp. Zool. **4**:447, 1907.

10. Stirling: J. Anat. & Physiol. **8**:402, 1874.

The limits of this paper will not permit a detailed description of the post-operative phenomena noted when individual or combined canals were opened. A brief resumé of the experimental findings will make clear the points I wish to emphasize:

When a *single horizontal* canal is removed, the pigeon is unable to maintain forward, linear equilibrium. He constantly falls to the injured side, turning toward the injured side. The head and eyes are slowly draw to this side, with the quick pull toward the unoperated side. No vestibular tremor is noted. Recovery takes place in ten to twenty-five days.

Removal of a *superior vertical* canal causes disturbance of equilibrium. The pigeon falls into the anterior quadrant on the side of the operation. There is a compound movement of the head; it is drawn upward and backward, then forward, downward, and to the opposite side. In flight, such a pigeon is able to fly upward, but will "side slip" anteriorly and downward into the anterior quadrant on the side of the operation. No vestibular tremor is noted. Recovery is rapid, taking five to eight days.

When a *posterior-vertical* canal is opened and the ampulla destroyed, the disturbance of equilibrium observed consists of falling backward into the posterior quadrant of the operated side. The nystagmus of the head and eyes is of a different type from that observed when the superior vertical canal is opened. The head is slowly drawn away from its perpendicular axis toward the injured canal, and then is quickly drawn back toward the opposite side. No vestibular tremor is noted. Recovery takes place in five to eight days.

When *both anterior (superior) vertical* canals are opened and their ampullae injured, the pigeon topples over forward into either the right or the left anterior quadrant. If *both posterior vertical* canals are opened, he turns over backward into either the right or left posterior quadrant. No vestibular tremor is developed, and recovery takes place in ten to twenty days.

Removal of *both vertical canals on one side* causes an equilibrium disturbance in both the anterior and the posterior lateral quadrants of the side of the operation. A slow pull of the head away from the perpendicular is seen with a quick pull toward the side of the operation. If the horizontal canal on that side is also opened, the head and eye nystagmus will be compounded and will alternate between horizontal and vertical, producing a third type which would be a rotary nystagmus.

When *both horizontal* canals are opened, I find that forward linear equilibrium is completely abolished. A very rapid head nystagmus of pendulum type develops. The head moves to the right and then to the left in a horizontal plane. There also develops a very fine, horizontal tremor (which I have designated "vestibular tremor), quite identical

in direction with the major head movement. The pigeon turns either to right or to left. After seven months the loss of forward linear flight is still greatly disturbed, the pigeon flying upward in cork-screw fashion. The head movement persists.

When both the *right anterior vertical and the left posterior vertical canals* are opened and the ampullae destroyed, the pigeon topples forward into the right anterior quadrant or backward into the left posterior quadrant. There is a rapid head nystagmus which may be pendulum in type, the direction of which is forward-downward to the left, and then backward-upward and to the right. A fine tremor is also noted, identical in direction with the major head movement. In attempting to walk or fly, the pigeon falls into either the right anterior quadrant or the left posterior quadrant. After months, the flight remains greatly disturbed, especially the control in the right anterior or left posterior quadrants.

When both the *left anterior vertical, and the right posterior vertical canals* are opened and the ampullae destroyed, the pigeon's head is drawn forward and the bill is directed toward the right. There is a rapid pendulum movement of the head forward, downward and to the right, and then backward, upward and to the left. A fine tremor of the head is noted, the direction of which is like the major head movement. In walking or in flight it topples forward into the left anterior quadrant, or falls backward in the right posterior quadrant. It will be noted that the movements in this case are exactly opposite to those of the preceding case. After six months the pigeon has not regained normal equilibrium.

When *all vertical canals* are opened and the ampullae destroyed, we should expect to find a combination of the phenomena of the last two experiments. That is exactly what happens. The head nystagmus may be downward, forward to the left, and backward, upward to the right, with a corresponding tremor, or the head nystagmus may be forward, downward to the right, and backward, upward to the left, with a corresponding tremor. These head movements are very rapid, and there is no definite manner in which they alternate. In walking or flight the pigeon may fall into any quadrant. Recovery has not taken place after five months.

From the foregoing it is evident that in all experiments in which there has been bilateral removal of the horizontal canals, of a right superior vertical and a left posterior vertical, of a left superior vertical and a right posterior vertical, or of all vertical canals—definite head nystagmus and a "vestibular tremor" have been observed. Pigeons with these operative lesions have not regained their normal motor co-ordination five to seven months after operation. They are unable to fly and the head movements persist; especially is this true with the

horizontal canals removed. In all other experiments (removal of any individual canal, anterior superior canals bilaterally, posterior vertical canals bilaterally, anterior and posterior vertical canals of the same side), recovery is more rapid. If all the canals of one side have been removed, the head is inclined toward that side. No tremor is noted. Twenty-five days after operation recovery of equilibrium has not fully taken place.

COMMENT

Head nystagmus in man has been observed by several investigators, but I find no cases reported in which mention is made of a fine head tremor accompanied by eye nystagmus in the same direction.

Mygrind [11] calls attention to head nystagmus in pigeons from irritation of the vestibular nerve endings, but adds: "It is otherwise in the human being: here a head nystagmus is of the greatest rarity." He examined fifty infants in a hospital in Copenhagen and found distinct facial reactions in most of them after rotation. In infants, aged 1½ months, he found a vestibular face reflex which consisted of a contraction of cheek muscles during rotation. In some, the left-hand corner of the mouth was drawn a little to the left and upward, with widening of the left palpebral fissure. Mygrind is greatly impressed with the head nystagmus in infants. He has collected four cases of head nystagmus in man. Ruttin [12] reports a case in which the head nystagmus was due to labyrinthine fistula. Urbantschitsch [13] observed two cases of head nystagmus due to labyrinthine fistula, one case being spontaneous. His observations are in accordance with the observations made by Bárány,[14] Alexander,[15] and Bartels.[16]

A review of the literature on tremors in general has brought to light no description of fine head tremors like those observed in the pigeons above described. Discussing human cases, Crenshaw [17] says: "With the exception of the tremors of Parkinson's disease, coarse tremors indicate organic changes. Fine tremors indicate toxic or functional conditions." I am not wholly in accord with this statement, inasmuch

11. Mygrind, S. H.: Head nystagmus in human beings, J. Laryngol. **36**:72, 1921.

12. Ruttin: Fistelsymptom und Kopfnystagmus, Verhandl. d. Oesterr. otol. Gesellsch. (Feb. 27) 1911.

13. Urbanschitsch, E.: Kopfnystagmus, Monatschr. f. Ohrenh. **44**:1, 1910.

14. Bárány, R.: Ueber einige Augen- und Halsmuskelreflexe bei Neugeborenen, Acta Oto-Laryngol. **1**:97, 1918.

15. Alexander: Die Reflexerregbarkeit des Ohrlabyrinthes beim menschlichen Neugeborenen, Zeitsch. f. Sinnesphysiol. **49**:153, 1910.

16. Bartels: Ueber Regulierung der Augenstellung durch den Ohrapparat, Arch. f. Ophth. **17**:1, 1910.

17. Crenshaw, H.: Tremor tracings, New York M. J. **103**:308, 1916.

as these vestibular tremors are fine and rapid, and they are certainly of organic origin in the experiments cited. Considerable interest therefore centers in the finding of several cases in the neurologic department of the Massachusetts General Hospital presenting fine head tremors and eye nystagmus identical in direction. Fourteen such cases have been noted to date and four of them are here summarized.

REPORT OF CASES

CASE 1. *Clinical History.*—J. S., a man aged 35, with negative family and personal history, came to the Massachusetts General Hospital Aug. 26, 1921, complaining of a pain in the chest and "shaking of the head." Four years before he had abscesses in several teeth and, soon thereafter, peculiar drawing sensations were noted in the muscles of the neck, and a peculiar rotary movement of the head. At that time he experienced pains in the region of the heart, general weakness, dull frontal headaches, shortness of breath, and objective vertigo accompanied by nausea. These symptoms have persisted with increasing severity, excepting the headaches, which at present cause no concern.

Examination.—The patient was of medium build, with a pinched, worried expression; the nasopharynx, heart and lungs were negative; the pulse was 80 and regular; the blood pressure was 130 systolic and 90 diastolic. The gastrointestinal and genito-urinary tracts were negative.

The only positive neurologic findings were: Right rotary nystagmus with the eyes to the right, and left rotary nystagmus with the eyes to the left; a fine tremor of the head, rotary in character, directed forward, downward to the right, and then upward, backward to the left. The eye nystagmus and head tremor were synchronous, and could not be dissociated.

The laboratory findings were: Urinalysis negative. Spinal fluid analysis: No cells; alcohol test negative; total protein 47 mg.; pressure 180 mm.; under jugular compression the dynamic tests were normal; Wassermann reaction negative. (After lumbar puncture the patient was confined to bed for one week with a severe post-puncture headache; during this time the rotary head tremors were greatly exaggerated and accompanied by intense vertigo, nausea and vomiting.)

Roentgen-ray examination of the teeth revealed: a buried upper right third molar; extensive bone infection around the root of the right lower first molar; an incompletely filled root canal in the left upper first bicuspid, with a small area of absorption at the tip. The third upper molar later was extracted, and an abscess was found.

Bárány tests were attempted, but not completed on account of distressing symptoms which developed during the examination and persisted with an increase in head movement for one week.

Comment.—The principal symptoms to which I wish to call attention in this case are the rotary head tremor and the rotary eye nystagmus, which are synchronous and cannot be dissociated. Another interesting fact is that recurrence of alveolar disease was coincident with exaggeration of the head tremor.

CASE 2. *Clinical History.*—O. G., a woman aged 41, with a negative family history, came to the Massachusetts General Hospital on account of "constant shaking of the head." Her health had been good until the age of 27, when she was confined to bed for five weeks on account of a left sided pleurisy.

During this illness the cavity was "tapped" several times. After three months the patient was able to go out of the house. Soon after this illness, "surging sensations" began in the head and left ear, and were followed by diminution in acuteness of hearing in the left ear. At times there was a lateral movement of the head, which was drawn to the left and rotated backward. When the head movements were increased, the patient experienced nausea and vomiting. These symptoms continued with little amelioration until 1918, since when they have abated somewhat. During the early part of 1918, the patient went to the Rutland Sanatorium on account of pulmonary tuberculosis. During this time a fine horizontal tremor of the head developed, and was accompanied by peculiar drawing sensations in the sternocleidomastoid muscles.

Examination.—Blowing respiration was observed in the apices of both lungs; the heart examination gave negative results; the pulse was 72; blood pressure systolic 120, diastolic 80; gastro-intestinal and genito-urinary tracts were normal.

The positive neurologic findings were: horizontal nystagmus when the eyes were turned to the right or left. A horizontal tremor of the head was present and was synchronous with the eye nystagmus, from which it could not be dissociated.

Hearing: Whisper not heard on either side; conversation on right 1/35, on left ½/35; upper limits, right 5, left 7; lower limits, right 96, left 512; Rinné test, right ½/24, left, 0/25; Weber test positive on both sides.

The triceps, biceps and radial reflexes were lively; the abdominal skin reflexes were not obtained; and the knee and achilles jerks and the plantar reflexes were lively.

Laboratory Findings.—The blood Wassermann reaction and urinalysis were negative. At a first examination of the spinal fluid the pressure was 103, there were no cells, the alcohol and ammonium sulphate tests were negative, total protein was 45, and the Wassermann test was mildly positive. At a second test the findings were: pressure 130, no cells, alcohol and ammonium sulphate tests negative, total protein 42, Wassermann test negative. Under jugular compression the dynamics were normal in both tests.

The Bárány and caloric tests were not satisfactory on account of extreme reaction to the slightest amount of stimulation by excessive nausea and vomiting. After the slight amount of vestibular stimulation, the patient was confined to bed for one week. The head tremors and drawing sensations in the sternocleidomastoid muscles were greatly increased after these tests.

Comment.—The outstanding symptoms in this case are, first: the horizontal eye nystagmus associated with the horizontal head tremor, which are synchronous and cannot be dissociated, and, second: the peculiar drawing sensations in the sternocleidomastoid muscles.

CASE 3. *Clinical History.*—J. J. O., a man aged 21, with negative family history, came to the Massachusetts General Hospital, May 10, 1922, on account of severe gastric pains. He had been operated on for cervical adenitis and an abscess in the left leg in early childhood, and had had jaundice four times, accompanied by a pustular eruption on the arms and body. He had a fracture of the left arm some years ago, and since had experienced difficulty in executing movements with this member without a great deal of incoordination. Three weeks before admission, he began to experience severe gastric pains, accompanied by nausea, vomiting and severe frontal headache. For three or four days he had been troubled with diplopia, strabismus and drowsiness.

Examination.—The general examination was negative. The positive neurologic findings were: diplopia due to paresis of the left external rectus muscle; double choked disk with swelling of 2 to 3 diopters; left horizontal nystagmus, greater in the right eye on account of the paresis of the left external rectus muscle; slight weakness of the left facial muscles; deviation of the tongue to the left; and bilateral ankle clonus.

The laboratory findings were: blood Wassermann reaction negative; urinalysis negative. The spinal fluid showed: xanthochromia, pressure 220 mm., pulse and respiratory oscillations good; jugular compression and cough produced good fluctuation; cells 12; alcohol and ammonium sulphate tests negative; total protein 50; sugar 0.0625; Wassermann reaction negative.

On May 13, while in the hospital, the patient noted that the air ventilator in the wall seemed to move slowly to the left, and then jump quickly back to its original position; this movement was repeated. A horizontal head tremor—synchronous with the eye nystagmus—developed simultaneously with the onset of the subjective movement of the ventilator on the wall. Unfortunately the patient left the hospital, May 16, against the advice of physicians.

Comment.—It is interesting to note that the patient is able to state definitely the time of onset of the horizontal head movement, and the simultaneous appearance of objects moving slowly to the left and then their quick return to the right.

CASE 4. *Clinical History.*—E. W., a woman aged 24, with a negative family history, came to the Massachusetts General Hospital, Aug. 21, 1922, on account of torticollis. Her health from infancy to the age of 22 had been good. During her twenty-second year, the patient had abscesses around three teeth. Soon thereafter, peculiar drawing sensations were felt in the muscles of the neck, especially the left sternocleidomastoid muscle, and a vertical tremor of the head was noticed. Since, she has had repeated attacks of torticollis.

Examination.—The general examination was negative with the exception of a chronic left torticollis, involving principally the left sternocleidomastoid muscle. The neurologic examination was negative except as follows: Vertical nystagmus upward, when looking upward, and a vertical tremor of the head synchronous with the vertical eye nystagmus.

The laboratory findings were: Urinalysis negative; blood Wassermann reaction negative.

In October, 1922, this patient returned to the clinic with the left side of the face swollen and tender, complaining of "toothache." The vertical tremor of the head and the left torticollis were greatly increased. After the swelling and inflammation had subsided, the head tremor and torticollis improved slightly.

Comment.—The interesting symptoms in this case are the vertical head tremors, and the vertical eye nystagmus (which are synchronous), the left torticollis, and the drawing sensations in the muscles of the neck. All of these followed abscesses of the teeth and increased with exacerbations of alveolar infection, which leads to the assumption of a possible causal relationship.

CONCLUSIONS

By the method briefly described, stimulation or destruction of an individual ampulla is easily accomplished; therefore it has been possible to make definite analyses of the functions of a single semicircular canal, and of various combinations of two or more canals.

Destruction of the ampulla of any one canal produces an eye nystagmus with head nystagmus in the same direction. Recovery of equilibrium takes place in from five to twenty days.

Destruction of the ampullae of both anterior vertical canals or both posterior vertical canals, or both vertical canals on one side, produces an eye nystagmus and a head nystagmus, identical in direction. Recovery takes place in each case in ten to sixty days.

Destruction of the ampullae of both horizontal canals, or of the left anterior vertical and the right posterior vertical canals, or of the right anterior vertical and the left posterior vertical canals, or of all the vertical canals, produces first an eye nystagmus, second a head nystagmus, and third a fine head tremor (which I have called a vestibular tremor). The direction of the three movements is alike in any one case. Recovery of equilibrium has not taken place six to seven months after operation.

Tremors of the head, accompanied by an eye nystagmus similar in direction, in fourteen cases in man, are comparable to tremors produced by vestibular operations on pigeons.

NEUROSYPHILIS IN THE AGED

A STUDY OF NINETEEN CASES OF SENILE NEUROSYPHILIS OCCURRING IN A SERIES OF 2,175 CASES OF ALL TYPES OF NERVOUS SYPHILIS *

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Judging by the total absence of American and English literature and the paucity of material on any forms of syphilis in the aged, neurosyphilis developing in old age has not interested many writers. A few American authors have noted its incidence or manifestations: Thom,[1] Wile,[2] and Sturgis.[3] Lucke,[4] in a study of 250 tabetics, reported two patients with earliest symptoms after 65 years. Tobias, Long and Cramer, Wilde and Thomas have reported cases developing in old age. Bumstead [5] years ago stated: "Syphilis contracted in old age is frequently a very serious disease. Tertiary lesions are prone to appear early and visceral and nervous complications are frequent."

Several French authorities have emphasized the severity of syphilis developing in the aged: Fournier, Dulac, Renault, Ricord and others. Gailleton [6] states that syphilis contracted after 60 years is nearly always rapidly fatal. Mendel [7] in his book mentions the fact that general paralysis occurs after 60 years only exceptionally. Recently Herschmann [8] of Vienna has studied general paralysis in the aged in Jauregg's clinic. In spite of this apparent lack of interest, the subject seemed to the writer to be one of great importance and a compilation of statistics on the incidence and manifestations of senile neurosyphilis worth while.

The records in the Philadelphia General Hospital and Hospital for Mental Diseases of all cases of neurosyphilis available since about 1915 were used. In approximately six years (the records during 1919 and

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* Read before the Philadelphia Neurological Society, April 27, 1923.

1. Thom, B. P.: Acquired Syphilis in the Aged, Med. Rec. **98**:730 (Oct. 30) 1920.

2. Wile, U. J.: Syphilis in Senility, Am. J. Syphilis **3**:193, 1919.

3. Sturgis, F. R.: Syphilis and Life Insurance, Med. Rec. **9**:161 and 217, 1874.

4. Lucke, Baldwin: Tabes Dorsalis, Pathological and Clinical Study of 250 cases, J. Nerv. & Ment. Dis. **43**:393 (May) 1916.

5. Bumstead and Taylor: Pathology and Treatment of Venereal Diseases. Ed. 5, Philadelphia: Lea & Febiger, 1883, p. 541.

6. Gailleton: Quoted by B. P. Thom; Footnote 1.

7. Mendel, E.: Textbook of Psychiatry Transl. by W. C. Krauss, Philadelphia: F. A. Davis Co., 1907.

8. Herschmann, H.: Med. Klin. **17**:1225 (Oct. 9) 1921; ab. J. A. M. A. **77**:2097 (Dec. 24) 1921.

1920 were not available), there have been about 2,175 cases of all types of cerebrospinal syphilis admitted to this hospital. For convenience these were divided into three groups, general paralysis (1,285 cases), cerebrospinal syphilis (492—including all types except tabes dorsalis) and tabes dorsalis (398 cases).

Many records of patients past 60 years of age with diagnoses of neurosyphilis were examined, but, on account of questionable ages, lack of confirmatory clinical, laboratory or necropsy findings, were discarded. Many of these, apparently, were cases of cerebral or cord arteriosclerosis, senile dementia or chronic nephritis complicated by alcoholism, prostatism, uremia, etc.

Statistics from a large charity institution, such as the Philadelphia Hospital, where, as a rule, the flotsam and jetsam of humanity are cared for, might not be in accordance with a similar group from another walk of life. But in a personal communication with Dr. F. G. Ebaugh, he stated that in a review of approximately 500 cases of general paralysis at the Trenton State Hospital he found none developing above 60 years.

The following features were particularly noted: age of onset (only those whose first nervous or mental symptoms occurred at 60 years or older were studied); the course and duration of the disease; the type of psychosis present; serologic tests; past history (particularly the age at which the initial lesion was contracted, with the period of latency until nervous symptoms were manifest and any other pertinent specific history present); and clinical symptoms and signs as well as results of treatment.

Of the total number, 2,175 cases, there were only nineteen, or 0.87 per cent., of cases in which the diagnosis of nervous syphilis with an onset at 60 years or older was certain. There were fourteen men and five women; two were negroes, one Belgian, one Austrian, one German and fourteen Americans.

Cerebrospinal Syphilis and Tabes Dorsalis.—In 802 cases of cerebrospinal syphilis and tabes dorsalis there were only eleven, or 1.3 per cent. (seven of tabes and four of cerebrospinal syphilis), developing at 60 years or older. Six of these 0.74 per cent. had their initial neurologic signs or symptoms at 65 years or above. These patients were all white; nine were men and two women.

(*a*) Onset: Four began with weakness of gait or ataxia; two with apoplexy; three with shooting pains; one with failing memory and one with incontinence. (*b*) Course of disease: In most instances this could not be determined, as some were discharged and a few patients remain in the hospital. (*c*) Serology: In three instances blood Wassermann reactions were negative and no spinal fluid tests were made. Three had positive blood with no spinal fluid examinations. The other

five had positive blood and spinal fluid Wassermann reactions. One patient with meningomyelitis had a general paralytic gold curve, but no clinical signs of general paralysis. (*d*) Age at which initial lesion was contracted; period of latency and results of treatment: in seven instances a history of a chancre was obtained, the youngest at 25 years, the oldest at 61 years. Two in the forties, two in the fifties and one in the thirties. It must be remembered that in this class of patients it is hard to obtain accurate histories of their early lesions. The earliest appearance of manifestations of nervous syphilis was one year. The longest period of latency was 35 years. The average period of latency was 18.5 years. All cases had typical signs of cerebrospinal syphilis, such as pupillary changes, reflex phenomena or other signs. In only three cases (27 per cent.) was any improvement noted with treatment.

General Paralysis.—(*a*) Onset: Of the 1,285 patients with general paralysis, eight, or 0.62 per cent. (two women and six men; two negroes and six whites), had the onset of their psychosis at 60 years or older. There was no proved case of general paralysis developing above 62 years. One case of cerebrospinal syphilis with psychosis developed at 64 years; three at 60 and four at 62 years. Five patients died in the hospital; the average duration of the disease in these was fifteen months, in comparison with the usual course of from two to six years. The most rapid termination was in six months, and none lived over two years after the onset of deterioration.

(*b*) Initial symptoms of psychosis: Three patients had as the first manifestations mental tension defects, such as memory lapses, confusion, disorientation, etc.; one began with apoplexy and headaches; one with excitement and delusions of persecutions; and one began with a suicidal attempt.

(*c*) Type of psychosis: In general, the type was that of simple dementia without delusions. Four patients showed nothing more. One only had the classic grandiosity; one was paranoid with ideas of infidelity (complicated by alcoholism). Two showed a pathologic sense of well-being with simple dementia.

(*d*) Serology: All patients had four plus Wassermann reactions in the spinal fluid; two had no records of blood tests. In six the blood was also positive. Four gave a general paralytic Lange reaction, one had a curve in the syphilitic zone, while the other three had no record of colloidal gold curves. Increased cell counts and globulin were reported in two instances.

(*e*) Past history: In only one case was a history of early lesions obtained; this patient had his secondary eruption at 62 years. Five patients gave histories of childless marriages or abortions. In two, no past history was obtainable. In three there was a history of chronic alcoholism. In these one had hallucinations of sight and one exhibited

paranoid trends. Their disease was of shorter duration and of more rapid deterioration than the others.

(*f*) Clinical signs: All patients showed typical general paralytic motor signs, such as facies, speech, tremors, disturbed reflexes and pupillary changes.

SUMMARY

Case records of 2,175 neurosyphilitics were examined. Only those with onset of nervous lesions at 60 years or older were studied; 1,285 were general paralysis, 492 cerebrospinal syphilis other than tabes, and 398 tabes dorsalis. The onset, age at which the initial lesion was contracted, period of latency, course of the disease, serology, type of psychosis and clinical symptoms and signs were studied. In nineteen authentic cases, 0.87 per cent. (fourteen men and five women), the disease developed after 60 years of age.

In 802 cases of cerebrospinal syphilis and tabes, 1.3 per cent. developed at 60 years or later; 0.74 per cent. at 65 years or older. Serologic tests confirmed the diagnoses in most instances and clinical signs in all. The average period of latency was 18.5 years. The chancre was contracted in most instances during middle life. In 73 per cent. of cases no improvement was noted with treatment.

Of 1,285 cases of general paralysis, 0.62 per cent. developed parenchymatous degeneration at 60 years or older. No patient in this series had an onset after 62 years. The average duration was fifteen months. The usual type of psychosis was simple dementia and resembled senile deterioration. Only one showed the usual grandiosity. Serologic tests were positive in all instances in spinal fluid and, in most cases, in the blood as well. General paralytic curves were reported in 50 per cent. of cases. As histories of initial lesions in general paralysis were not obtainable, periods of latency could not be determined. Paranoid trends were not conspicuous in this series of senile general paralysis, as they were in Herschmann's [8] cases. Patients with chronic alcoholism had a more rapid course. This accords with observations of Sturgis,[3] Kaposi,[9] Blaschko [10] and others. All patients had typical clinical signs of general paralysis.

CONCLUSIONS

1. Cerebrospinal syphilis and tabes dorsalis developing in senility (60 years or older) are rare because in most cases the chancre is contracted in early life. The incidence is approximately 0.5 per cent. of all neurosyphilis cases. Aged patients suffering from cerebral

9. Kaposi, P.: Pathologie und Therapie der Syphilis, Stuttgart: Enke, 1891, p. 496.

10. Blaschko, A.: Syphilis and Life Insurance, Med. Exam. and Pract. **14**:593, 1904.

arteriosclerosis, senile deterioration or nephritis are at times mistaken for neurosyphilis. Cases developing after 60 years usually have the initial sore in middle life. In a few instances there appears to be a long period of latency, then, in the metamorphosing stage, this immunity is broken down, probably as a result of the degenerative processes of age. Then the neurosyphilitic involvement becomes apparent, and, as a rule, does not respond to treatment, but is rapidly fatal.

2. General paralysis developing in senility is rare, 0.62 per cent., and frequently is confused with senile dementia. General paralysis practically never develops after 65 years. We agree with Herschmann [8] that general paralysis in seniles simulates closely the dementia of senile deterioration. The termination in senile cases is hastened approximately 50 per cent.

DISCUSSION

DR. FRANCIS X. DERCUM: I think it is a matter of common experience that syphilis acquired in middle life is very resistant to treatment. I think that is true both of the gummatous and parenchymatous forms. Syphilis acquired in middle life is controlled with great difficulty and is likely to be followed by rapid deterioration of the individual. General paralysis is due usually to an infection acquired in early life and it therefore makes its appearance long before old age is reached. At the same time I have records of several cases of very long interval between the initial lesion and the occurrence of symptoms. I have one record in which the initial lesion was said to have been contracted forty-two years before. In such a case, the patient immunizes himself for a long time, but, as the years pass by, his resistance wanes and the occasional spirochetes, lurking quiescent in his tissues, become active.

THE FACTOR OF DETERIORATION IN CHILDREN SHOWING BEHAVIOR DIFFICULTIES AFTER EPIDEMIC ENCEPHALITIS *

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The twenty patients on which this study is based were referred to the Institute for Juvenile Research by physicians, school authorities, or parents, chiefly because of incorrigibility, poor memory, or deterioration of general intelligence. Physical, psychologic and psychiatric examinations were made in each case with special emphasis on the psychologic factors involved. Preceding the attack of encephalitis, behavior difficulties were either absent or of little significance in each case. The first examinations were made two months to three and one-half years after the attack of epidemic encephalitis, the average being twenty-two months. The second examinations were made two to twenty-one months after the first, the average being six months; the third, an average of eleven months after the first examination.

In the literature on epidemic encephalitis in children, most writers conclude that when mental changes occur after the disease they consist of one or more of the following: (1) deterioration of intelligence; (2) definite attention disorders; (3) deterioration of memory, and (4) emotional disturbances. Most writers regard the intelligence deterioration, including deterioration of memory and attention as of more importance than the emotional disturbance. Barker [1] states, "one of the saddest of the sequels of epidemic encephalitis, especially in children, is mental deficiency. Unfortunately a considerable proportion of the children attacked are rendered permanently deficient. All grades of this deficiency from outspoken idiocy to slight backwardness have been observed in this country and Paterson and Spence report similar experiences in England. Even in adults deterioration with loss of memory and defective judgment may occur." Grossman [2] found

* Read before the Chicago Neurological Society, March 15, 1923.

1. Barker, L. F.: Sequelae of Epidemic Encephalitis, New York State J. M. **22**:251 (June) 1922.

2. Grossman, Morris: Sequels of Epidemic Encephalitis, J. A. M. A., **78**:959 (April 1) 1922.

that "failing memory, especially for recent events was a common complaint. When they read they found it difficult to concentrate and they soon forgot what they had been reading about." Buzzard [3] states: "I am convinced that a large number of cases of epilepsy, of mental deficiency, . . . are the permanent results of encephalitis in childhood." Paterson and Spence [4] conclude: "The results of mental states following encephalitis in children may vary from complete idiocy to slight mental deficiency." S. R. Leahy and I. J. Sands [5] in their summary of the changes after encephalitis mention definite attention disorders. Joseph B. Neal [6] noted definite mental deterioration in many of his cases. However, in the literature cited, there is no statement of the type of attention disorders and emotional changes, nor a measure by standard tests of the deterioration in intelligence. Presumably the conclusion that deterioration occurred, and was in some cases progressive, was based on the school maladjustment, the behavior difficulties and the changes in personality.

The diagnosis of mental deterioration is probably often based on findings that result entirely from the physical defects. This was well illustrated in one of our patients, who was excluded from school because of his inability to write quickly and legibly, his slowness in responding to questions and the disturbance he created in the school room. Before the illness with encephalitis he did well in school. The school authorities and family physician reported that the boy's intelligence had deteriorated to such a degree that they were considering placing him in the subnormal room. Psychometric tests showed that the boy's intelligence was above the median for his grade. This case is typical of many referred by local physicians and school authorities because of "mental deterioration."

In our cases no evidence of deterioration of intelligence was revealed by psychometric tests. Some patients presented an appearance of dulness that was due to the apathetic facial expression. The only mental disturbance in these patients was emotional. Irritability, outbursts of temper, quarrelsomeness, frequent changes of mood, and in a few cases marked emotional indifference were observed. The reactions and responses to similar situations were extremely irregular from one time to another. The patient would be alert, paying attention and showing

3. Buzzard, E. F. and Greenfield, J. G.: Lethargic Encephalitis; Its Sequelae and Morbid Anatomy, Brain, **42**:305 (June) 1920.

4. Paterson, D. and Spence J. C.: After-Effects of Epidemic Encephalitis in Children, Lancet, **2**:491 (Sept.) 1921.

5. Leahy, S. R. and Sands, I. J.: Mental Disorders in Children Following Epidemic Encephalitis, J. A. M. A., **76**:373 (Feb.) 1921.

6. Neal, Joseph B.: Experience with more than 100 Cases of Epidemic Encephalitis in Children, J. A. M. A., **77**:121 (July 9) 1921.

interest, when suddenly a lapse would occur during which he scowled and seemed angry. During the next lapse the patient might smile, laugh or appear quite merry. This was especially observed during the psychometric examinations. The patients, with two exceptions, were usually alert and hyperactive, and their replies to questions were quick and to the point. It is important to note that three cases had been wrongly diagnosed manic-depressive psychosis—manic phase—because of the restlessness, hyperactivity and emotional instability. One case had been diagnosed hysteria, and one "severe psychoneurosis."

The degree of behavior difficulty in our cases was not proportional to the physical findings. One of our most difficult behavior problems was in a patient who, following the encephalitis, developed merely a slight tremor of the hands.

All of our twenty patients were given a complete Stanford-Binet intelligence examination and supplementary tests. The latter included: the cancellation of *A;* Franz dot-tapping; Seguin form board; Healy puzzles *A* and *B;* Healy picture completion tests 1 and 2; Porteus; and Knox cube tests. The range of chronologic ages was from eight to seventeen years, the average being eleven and one-half years. The range of intelligence quotients was 71 to 121. Four were classified in the borderline group; six, dull and backward; nine, adequate intelligence; and one, superior intelligence.

One of the specific reasons given for the examination was poor memory. In most cases this was the most serious complaint. Several parents stated that the child was unable to remember specific orders for as short a period as five minutes. The psychologic examinations, however, failed to reveal any memory defect in these or other cases. There were no failures in memory tests for sentences, passages or digits in more than one year below the mental age scored and successes were obtained in year levels above the mental age in all but three cases.

Similar results were obtained with tests of attention. The cancellation of *A* and the Franz dot-tapping tests, as well as those Stanford-Binet tests in which attention is an important factor, such as the rote memory tests, arithmetical reasoning, clock tests, etc., revealed, in every case, successes compatible with the mental age of the patient. This was true, however, only when the patients were calm and cooperative. Although the attention was within the range of normal as measured by the tests, marked fluctuations always occurred. These always accompanied, and were apparently caused by, an obvious emotional disturbance. There was apparently no disturbance in the subjective or objective conditions of attention except for the inhibition due to the emotional disturbance. There was, for example, a delay of several seconds in responding to a question previously answered correctly. One patient gave a good introspective description of the difficulty by

saying several times during the examination, "I know the answer but have forgotten it. Wait a minute." During these intervals—often lasting but fifteen to forty seconds—the patients appeared restless and excited. In two cases, these periods were accompanied by flushing of the face and an apparent inability to respond. During the longer intervals some of the patients had attacks of polypnea, stood up and often became very irritable. This disturbance varied in character and intensity in the same individual and occurred during periods of emotional disturbance only. This delay in response did not become greater as time went on, in spite of an increasing physical impairment in some cases.

No intelligence tests were given before the attack of encephalitis. However, in all cases, the mental ages correlated well with records in the public schools previous to the illness. Twenty re-examinations did not show a decrease in the intelligence quotient in any case, in spite of increasing behavior difficulties and school maladjustments. When school difficulties were investigated, it was found that the teachers complained chiefly of incorrigibility and lack of application. This apparently accounted for the failure to accomplish the work of the grade.

CASE SUMMARIES [7]

CASE 1.—S. H., a boy aged 14, who had had encephalitis in November, 1919, was referred in November, 1921, because of expulsion from the public school as "unfit to be among school mates." Complaints by the teacher were constant muttering, facial grimaces, repetition of questions, outbursts of temper, and fighting with the other children. The mother stated that "the patient could not sit still at home. He is constantly moving, talking and grimacing. If he is not talking he must be chewing something. He sleeps a great deal in the day-time."

Physical examination revealed: a well developed boy; pupils unequal and sluggish; drooling; tremor of hands and facial muscles; deep reflexes exaggerated; bilateral Babinski reflexes; cogwheel resistance of the arms; blood and spinal fluid Wassermann tests negative; optic disks negative. A second examination in May, 1922, and a third two months later gave practically the same findings.

Psychiatric examination revealed chiefly restless activity and emotional instability. Two later examinations showed practically the same behavior. He appeared anxious to get well, and could not explain his sudden outbursts of temper.

Psychometric Examinations.—November, 1921: Mental age, thirteen years two months; intelligence quotient, 98. May, 1922: intelligence quotient, 98; educational tests were passed up to his grade. Psychometric rating: adequate intelligence; no memory defects. During both examinations the cooperation was good between the periods of emotional disturbance. During these periods, which varied in length and severity, the reaction time was irregular—sometimes

7. These are of necessity very brief and contain only facts pertinent to this investigation.

very short, but usually long. There was apparently much difficulty in thinking as evidenced by the increased reaction time, the frequent interpolations, "I don't know" or "I can't think that," and later giving the correct response. During these periods of emotional upset the attention was unsustained. The patient would often stop suddenly during a response and continue a moment later with an irrelevant remark. In two such instances he stopped in the middle of a response and finished the answer to a previous question.

The boy's behavior difficulties increased after the second examination. At one time he hit a member of the family with a gas-pipe. The parents were unable to cope with the boy, and the only recourse was to send him to the Psychopathic Hospital. From there he was sent to a state hospital.

CASE 2.—M. B., a girl aged 14 years 5 months, who had had encephalitis in January, 1920, was referred, Feb. 24, 1920, because of physical disturbances and behavior difficulties that dated from the time of the illness. She had been expelled from school because of fits of temper, crying spells, and fighting with other children. Before the illness she was described as the "pet of the neighborhood." After the illness she had violent fits of temper, fought with children in the streets and with the neighbors, threw dishes, etc. at her grandparents, mistreated a smaller brother, choked chickens to death, and twice attempted suicide by turning on the gas. Physically she was well developed; the pupils were somewhat irregular but reacted well to light and in accommodation; the tongue deviated to the left; there was right facial paresis and spasm of the left facial muscles; speech was slurring; the hands were moist and cyanotic; otherwise the examination was negative. A second examination, five months later and a third, ten months later, gave similar findings. The patient was very active and alert; there was marked emotional instability and she cried frequently. At times she was cooperative and volunteered information regarding alleged mistreatment at home. At other times she was irritable and displayed a violent temper. The psychiatric examinations, five and ten months later, showed practically no change.

Psychometric Examinations.—On the date of admission: Mental age, eleven years, four months; intelligence quotient, 79. Five months later: intelligence quotient, 81. Ten months later: intelligence quotient, 81. The attention and memory tests were adequate for the mental age. During the tests there were periods of emotional outbreak, with at times apparent inability to think clearly. She stated several times, "I just can't get my mind on it." Between these periods, cooperation was good and tests failed during the emotional upsets were done correctly. The digit tests of year XII, and the arithmetic tests of year XIV were done correctly.

Since the patient's behavior was unimproved after the second examination, it was necessary to commit her to a state institution. There she has been very difficult to control at times, and on one occasion struck and injured the matron.

CASE 3.—G. M., a boy, aged 10, who had encephalitis in the Spring, 1921, was referred Sept. 20, 1921, because of incorrigibility, insomnia, outbursts of temper and fighting with other children. Physical examination revealed tremor of the hands, muscular irritability, and frequent spells of polypnea. The Wassermann reaction was negative. During the psychiatric examination he was irritable and excitable, panted a great deal at times, but cooperated well. He was brought back July, 1922, because he attacked the mother with a butcher knife. He was sent to the Psychopathic Hospital and transferred to the Lincoln State School and Colony. Before the illness he had been in low second grade at school.

Psychometric Examination.—Sept. 20, 1921: Chronologic age, ten years, three months; mental age, seven years, two months; intelligence quotient, 70. March 22, 1922: Chronologic age, ten years, nine months; mental age, seven years, ten months; intelligence quotient, 72; tests for memory and attention passed in year IX.

CASE 4.—R. B., a girl aged 10, who had had encephalitis in January, 1918, was referred March 15, 1921, because of disobedience at home and in school, fighting with children, outbursts of temper, and inability to learn in school. Physical examination revealed: right divergent strabismus, unequal pupils with sluggish reaction to light, tremor of hands and tongue, and exaggerated deep reflexes. The Wassermann reaction was negative. Previous to the encephalitis the patient had been in low first grade at school and gave no trouble. Psychiatric examination showed chiefly irritability, excitability, hyperactivity, restlessness, and talkativeness. During the second examination December, 1922, at the Geneva State School for Girls, she was irritable, but cooperative. The physical examination showed no change, except for increased tremor of the hands.

Psychometric Examinations.—March, 1921: Chronologic age, ten years, six months; mental age, nine years; intelligence quotient, 86. The second examination showed: mental age, eleven years, four months; intelligence quotient, 91; cancellation test, year XII; dot-tapping, adequate. During the second examination she often started to give a response, then suddenly stopped, giving it correctly a few minutes later when responding to a different question.

CASE 5.—E. S., a girl aged 12, who had had encephalitis in November, 1920, was referred July 19, 1921, because she had been in bed three weeks, and had "spells during which she did not know what she was doing. Cries and bites people." The patient was described by school teachers, mother and grandmother as "obedient, respectful and a good worker" before the illness. After the illness she changed from a smiling docility to a very excited and irritable girl. She often fought and struck at people about her.

Physical examination revealed: a poorly developed girl with unequal pupils, exaggerated deep reflexes, and later nystagmus. A second examination, Oct. 29, 1921, showed no changes except a greater inequality of the pupils. The blood and spinal fluid Wassermann reactions were negative. Examination, Dec. 7, 1921, showed no change. During the psychiatric examination, the patient responded and reacted well, except for periods of excitement, during which she had deep breathing spells.

Psychometric Examinations.—July 19, 1921: Chronologic age, twelve years, two months; mental age, ten years, two months; intelligence quotient, 83; she cooperated well until year XIV was reached, and then became excitable; form board, seven years; Healy puzzle "A," ten years; Healy picture completion, No. 1, adult; Porteus maze, eleven years. Dec. 14, 1921: Mental age, eleven years, nine months; intelligence quotient, 93. She had several seizures of polypnea and excitement, but between these periods she responded well. She failed in several tests during the deep breathing spells which were later done correctly. Problems and clock tests, of year XIV, were done correctly.

The patient gradually improved in behavior, and in February, 1923, was giving little trouble at home. The periods of excitement were less in number and intensity; and she was doing satisfactory school work.

CASE 6.—M. S., a girl aged 14, who had had encephalitis in March, 1920, when she became cross-eyed and slept for three weeks, had no behavior trouble before this illness, was referred with complaints that she was irritable, quarrel-

some, struck people without cause, and was a disturbing element in school. She had been in the seventh grade and did well in school before the illness. Physical examination revealed divergent strabismus, sluggish pupillary reactions to light and coarse tremor of the tongue which deviated to the right. The psychiatric examination revealed: Hyperactivity, emotional shallowness, giggling and laughing at questions.

Psychometric Examinations.—March, 1920: Chronologic age, fourteen years, ten months; mental age, thirteen years, ten months; intelligence quotient, 93; arithmetic and clock tests for the year XIV were done correctly. March 3, 1923: Chronologic age, fifteen years, seven months; mental age, fourteen years, nine months; intelligence quotient, 94; cancellation "A" test, fifteen years; dot-tapping, regular. She repeated six digits backward. There were several outbursts of laughter and some irritability during the tests. Although school grades were satisfactory, the girl was excluded a few months before completing the eighth grade because of her behavior.

Case 7.—I. F., a girl aged 12, who had encephalitis in June, 1919, was referred Feb. 15, 1922, because she slept most of the day and was incorrigible. Physical examination revealed: left pupil larger than the right, deviation of the tongue to the right, slurred speech, and exaggerated deep reflexes. The Wassermann reaction was negative. Psychiatric examination revealed: evasion; answers of the type "I don't know" to most questions. A second examination Jan. 16, 1922, showed similar reactions. Previous to the illness, the patient attended school for two years, but failed to pass into the second grade.

Psychometric Examinations.—Feb. 15, 1922: Chronologic age, twelve years, three months; mental age, nine years, two months; intelligence quotient, 74. April 14, 1922: mental age, nine years, four months; intelligence quotient, 74. June 16, 1922: intelligence quotient, 72. Designs and memory test of year X were done correctly at all examinations.

Case 8.—E. P., a boy aged 4, who had encephalitis six months before, was referred Sept. 28, 1921, with complaints of stubborness, defiance, crying spells, and frequent outbursts of temper. Physical examination revealed chiefly weakness in one upper extremity and exaggerated deep reflexes. The Wassermann reaction was negative. Psychiatric examination revealed chiefly irritability and "explosive reactions."

Psychometric Examinations.—Chronologic age, three years, eleven months; mental age, three years, four months; intelligence quotient, 85.1. Nov. 9, 1922: mental age, four years, four months; intelligence quotient, 85.2; memory tests of year IV were passed. Cooperation during the second examination was good. He was less irritable and in general his behavior had improved.

Case 9.—H. H., a boy aged 9, who had encephalitis in December, 1919, was referred Feb. 24, 1922, with complaints of restlessness, nervousness, outbursts of temper, and minor delinquencies. "When in a temper or fighting mood he may hit anyone with whatever he may happen to have in his hands." The school record was: "Entered first grade in 1918. A bright boy. After his illness there was a marked change. He was sullen, passionate and nervous; and learned with difficulty. He also had spells of deep breathing." Physical examination revealed exaggerated deep reflexes, stuttering of speech, and occasional attacks of polypnea. The Wassermann reaction was negative. Psychiatric examination revealed chiefly restlessness, irritability, irregular periods of resistance to questioning, and emotional instability.

Psychometric Examinations.—Mental age, eight years, four months; intelligence quotient, 90. The attention was irregular during the periods of deep breathing and during the emotional outbursts. He frequently gave correct responses to questions previously answered incorrectly. There were several periods of marked delay in responding to question during which the patient stared at the examiner. The examination, ten months later, showed: Mental age, nine years, six months; intelligence quotient, 94. Attention was good except during periods of emotional instability when there was marked delay in responses. At one time, testing had to be stopped for fifteen minutes during which the patient appeared extremely angry, threw objects on the floor and had a spell of deep breathing. Later the testing was resumed with full cooperation and the responses were average for the age.

Case 10.—I. D., a boy aged 16, who had encephalitis in February, 1922, was referred Sept. 28, 1922, with a history that before this attack he was "full of life and ambition and devoted to his family; since, he has lost interest in his family, personal appearance and study; is irritable and has unreasonable desires; becomes exhausted and drowsy; is unable to hold positions because of drowsiness while at work." Physical examination revealed unequal, sluggish pupils, paresis of the external rectus of the right eye, tremor of the hands and markedly exaggerated deep reflexes. Frequent reexaminations up to March 6, 1923, showed a gradually lessening tremor of the hands, but otherwise no change. The Wassermann reaction was negative. Psychiatric examination revealed: marked emotional indifference; continuous smiling even when the examiner purposely reprimanded him. There were frequent flights of attention and hyperactivity.

Psychometric Examinations.—Mental age, sixteen years, one month; intelligence quotient, 101. There were irregular periods of talkativeness, accompanied by elaboration; the attention was not sustained, and he appeared amused at the examination. March 6: Mental age, seventeen years, six months; intelligence quotient, 109; cooperation good; he repeated seven digits backward and eight digits forward; the ingenuity test in year XVIII was done correctly; cancellation "A," sixteen years; dot-tapping, regular.

Case 11.—J. K., a boy aged 11, had encephalitis in November, 1919, and was referred Jan. 23, 1923, with complaints of incorrigibility, frequent outbursts of temper and fighting with playmates, and attempts to strangle several children. He had difficulty in school previous to the illness. Physical examination revealed: chiefly, exaggerated patellar reflexes, and very slight tremor of the hands; the Wassermann reaction was negative. Psychiatric examination revealed: chiefly, emotional instability and a marked indifference to the accusations. He persisted in stating he "just didn't know why he did those things."

Psychometric Examination.—Chronologic age, eleven years, four months; mental age, eight years, ten months; intelligence quotient, 78.

Case 12.—G. L., a girl aged 11, had had encephalitis in June, 1918, and was referred Feb. 9, 1922, with complaints of muscular twitching, restlessness, frequent loss of temper, incorrigibility and spells of deep breathing. Physical examination revealed: pupils slightly irregular, coarse tremor of the tongue and hands; active reflexes; the Wassermann reaction was negative. Psychiatric examination revealed chiefly marked changes of mood, irritability and hyperactivity.

Psychometric Examinations.—Dec. 3, 1921 (at the public school): Mental age, seven years, two months; intelligence quotient, 67. Feb. 9, 1922: Chrono-

logic age, ten years, ten months; mental age, seven years, ten months; intelligence quotient, 71; school tests showed school ability of the low second grade.

CASE 13.—L. M., a boy aged 12, who had encephalitis in November, 1919, and was referred Sept. 17, 1921, because of wandering away from home, incorrigibility and stealing. Physical examination revealed the pupils to be slightly unequal, the left larger than the right, and a slight tremor of the hands. Reexaminations showed no change. The Wassermann reaction was negative. The psychiatric examinations revealed marked egocentricity, evasiveness, and resistance to questioning.

Psychometric Examinations.—Sept. 17, 1921: Chronologic age, eleven years, eight months; mental age, fourteen years, two months; intelligence quotient, 121; Trabue test, fourteen years; Pintner test, fourteen years, six months; Healy picture completion, No. 2, thirteen years; Form board, thirteen years. He repeated six digits backward. Aug. 10, 1922: Chronologic age, twelve years seven months; mental age, seventeen years, two months; intelligence quotient, 136. He repeated eight digits correctly, and also scored the ingenuity test for the year XVIII.

CASE 14.—F. K., a boy aged 17, who had encephalitis in 1919, and was referred Jan. 5, 1923, because of incorrigibility and violent temper. He had been at a state hospital from October, 1921, to June, 1922. His school record showed that the boy was doing poor work in the sixth grade before the illness. Physical examination disclosed: the posture stooped with hands immobile at the sides; gait slow, the left foot being dragged; marked propulsion and retropulsion; tremor of the head; paresis of the right external rectus; irregular pupils with sluggish reaction; slight facial paresis; reflexes exaggerated; tremor of tongue and extremities; muscular rigidity. Psychiatric examination in October, 1921, showed the patient to be alert, irritable and excitable. He became very angry at the least provocation; readily admitted the misbehavior, but gave no reason for it. Examination Jan. 19, 1922, showed similar reactions.

Psychometric Examination.—January, 1923: Chronologic age, sixteen years, nine months; mental age, ten years, ten months; intelligence quotient, 80; Knox cube test, twelve years; repeated seven digits; Healy picture completion, No. 1, twelve years; Healy picture completion, No. 2, sixteen years.

CASE 15.—L. B., aged 8, who had been ill in February, 1922, the nature of the illness being vague, though the mother stated that he had a fever (influenza), after which he slept for two weeks, and that a diagnosis of nephritis had been made, was referred Oct. 13, 1922, because he had become irritable, ran away from home, stole money from home and strangers, had become very forgetful and caused much trouble in school. There was no behavior difficulty before the illness. The patient was in the second grade of school. Physical examination revealed a left divergent strabismus, the left pupil was irregular and larger than the right and both pupils reacted sluggishly to light. Otherwise the findings, including the Wassermann reaction, were negative. Psychiatric examination disclosed that the patient was alert and interested; he was very restless and talked continually; he readily admitted the behavior difficulties.

Psychometric Examinations.—Chronologic age, eight years, six months; mental age, seven years, eleven months; intelligence quotient, 93; attention and memory tests were passed for the year above the mental age; Sequin form board, eight years; Pitner directions, seven years; Healy puzzle A, seven years; Healy picture completion, No. 1, eleven years. The second examination,

March 10, 1923: Mental age, nine years, four months; intelligence quotient, 104; the cooperation was very good; the restlessness and irritability were less noticeable.

CASE 16.—C. M., a girl, aged 12, who had encephalitis in February, 1919, was referred because of behavior difficulties at home and in school, and the parents were unable to control her. Physically: The expression was dull; speech was stuttering; there was slight ptosis of the eyelids; the knee jerk was present on the right, absent on the left; there was a coarse tremor of the head; otherwise the findings were negative. Psychiatrically, Jan. 20, 1921: The girl was generally alert and interested; at times she was restless, but answered questions correctly and to the point. Later examinations, Jan. 3, 1922, and April 10, 1922, gave the same results excepting for increasing irritability.

Psychometric Examinations.—Jan. 20, 1921: Chronologic age, twelve years; mental age, ten years; intelligence quotient, 83. Jan. 3, 1922: Mental age, ten years, two months; intelligence quotient, 78. April 10, 1922: Intelligence quotient, 76. Attention and memory tests were adequate for the mental age in all examinations.

Because of the increasing behavior difficulties, the patient was admitted to the Psychopathic Hospital after the third examination. From there, because of a mild psychosis, she was committed to a state institution.

CASE 17.—B. W., a boy, aged 12, was referred because of behavior difficulties at home and in school, "childishness and nervousness." The parents stated that the patient became very much excited and screamed without specific cause. There was no history of encephalitis, but six months before admission the patient complained of periods of sleeplessness. Two and one-half years before that he was ill for about two weeks. No diagnosis was made at that time. After the illness, for about one year, he was extremely drowsy through the day. Before the illness the boy did good work in the fourth grade at school.

Physical examination revealed: The left nasal labial fold smooth; paresis of the right lower facial muscles; right convergent strabismus; pupils equal, somewhat irregular, and reacting sluggishly to light; a coarse tremor of the hands and fingers; slight resistance to passive motion in the right arm and marked resistance to passive motion in the lower extremities; deep reflexes exaggerated, but equal on the two sides; a positive Babinski reflex on the right side; Oppenheim and Gordon reflexes doubtfully positive on the right; abdominal and cremasteric reflexes diminished; the speech heavy, coarse and slow. Psychiatrically, the patient was restless, irritable, and hyperactive; his responses were quick, and he stated that he "got so mad he couldn't stand and didn't care what he did at those times."

Psychometric Examination.—Mental age, twelve years, four months; intelligence quotient, 103; the box test of year XVI and digits tests of year XII were done correctly; the dot-tapping was regular.

CASE 18.—J. Z., a boy, aged 19, who had had encephalitis four years before admission, was referred for mental rating and vocational advice. He had graduated from the eighth grade in school since the illness.

Physical examination, March 8, 1923, revealed: Posture stooped; gait rigid; some propulsion; marked retropulsion; marked tremor of the hands, arms and legs, more on the right side; tremor of the head at times; movements slow and difficult; legs spastic; paresis of the right facial muscles; divergent strabismus of the left eye; pupils irregular, unequal, and with sluggish reaction to light; Wassermann reaction negative. Psychiatrically, the patient was dull and

apathetic; his responses were logical; he complained that he was unable to get work since the illness, his parents and other members of the family did not want him around because of his physical condition, and he was not allowed to eat at the same table as other members of the family.

Psychometric Examinations.—June 8, 1922: A Stanford-Binet intelligence examination was given by the Child Study Department; intelligence quotient, 86. March 8, 1923 (date of admission): Mental age, fifteen years, nine months; intelligence quotient, 97.

CASE 19.—G. R., a girl, aged 17, was taken to the Detention Home, Aug. 18, 1919, because of incorrigibility and staying away from home. The behavior difficulty dated from influenza in the late summer, 1919. She was sick in bed for three weeks, was delirious one day, was very sleepy during the illness, and was weak and drowsy after the illness. During convalescence she saw double and complained of stiffness, especially of the face and throat. She stated: "My face and eyes got a dull look after the illness." The patient was sent to a girls' school in 1920. Physical examination revealed: Left internal strabismus, right facial paresis, stiffness of the right side of the face, coarse tremor of the fingers, and Wassermann reaction negative. Psychiatrically, the patient appeared dull and indifferent; she smiled frequently; had no plans for the future; and had frequent quarrels at the school.

Psychometric Examinations.—Aug. 18, 1919: Mental age, twelve and one-fifth years (by the 1911 Binet scale). January, 1920: Mental age, fourteen years, eleven months; intelligence quotient, 93. February, 1923: Mental age, fourteen years, eleven months; intelligence quotient, 93; attention and memory tests were passed for the year beyond the mental age in the last two examinations.

CASE 20.—M. F., a boy aged 16, who had had two attacks of influenza a year and one-half before, was referred to the institute because of incorrigibility, stealing and threatening suicide. There was little behavior disturbance before the influenza. He had finished the first year in high school before the illness. Physical examination revealed: slight left facial paresis; right pupil slightly larger than the left; the knee jerks exaggerated, much more on the right than the left; other deep reflexes exaggerated; cremaster reflexes sluggish on both sides; and the Wassermann reaction negative. Psychiatric examination showed chiefly: marked changes of mood, irritability, stubborness, and periods of apparent anger.

Psychometric Examination.—March 7, 1923: Mental age, fifteen years, nine months; intelligence quotient, 98; the box and memory tests of year 16 were done correctly; Healy picture completion "A," 16 years.

SUMMARY

Since August, 1919, of 1,370 cases referred to the Institute for Juvenile Research because of behavior difficulties, twenty were directly traceable to epidemic encephalitis. There was a record of delinquency preceding the disease in only two of these cases. In both, the behavior difficulty was markedly aggravated by the disease. The complaints were chiefly: incorrigibility and uncontrollable temper in ten cases; sex delinquency in four cases; poor memory in two cases; and mental deterioration in three cases. The most frequent findings were: irritability, outbursts of temper, constant fighting and quarrelsomeness.

By psychometric tests the twenty cases were classified as: borderline defective, 4; dull and backward, 6; adequate intelligence, 9; superior intelligence, 1. Three examinations at intervals averaging eleven months were made in four cases; two examinations after intervals averaging six months in sixteen cases; a single examination in four cases.

Evidence of a psychosis was noted in one case.

No deterioration of intelligence, as measured by psychometric and educational tests, was present in any case. This is in striking contrast with the manifest behavior and the appearance of the patients.

No memory defects were apparent for school attainments; and retention, as measured by tests, was in keeping with the mental age.

Though marked fluctuations of the attention processes occurred, there was no evidence of defect in attention between these periods. These fluctuations were always in relation with some disturbance of affect.

Inhibition of responses was noted frequently during the examinations. This occurred irregularly during periods of mild emotional disturbance and while cooperation was good. This inhibition usually manifested itself by inability to give or finish responses previously or later given correctly.

There was no apparent relation between the severity of the conduct disorder and the severity of the physical defects.

Of these cases, seven have been excluded from school because of behavior disturbance. Of the ten who continued in school, seven were promoted and three failed to pass to the next grade. In all cases there were many absences because of the disease and marked lack of application due to emotional disturbance while in the classroom. Three of the children were excluded from school because of behavior disturbances after having been promoted at least one grade.

Follow-up investigations for an average of three years after the onset of the illness were made on sixteen cases. Ten patients showed unimproved or worse behavior; six showed slight improvement; three showed markedly improved behavior.[8]

DISCUSSION

DR. BEVERLY: Many observations were made and questions arose during psychologic examinations of these patients which have not been directly included in the paper. The influence of the emotional changes on the other mental processes and the educational status of the children are possibly the most important and interesting problems.

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8. We wish to express indebtedness to Irene Case Sherman and other psychologists at the Institute for Juvenile Research for aid in giving psychologic examinations and suggestions, and to Miss Blanche Cole for the social service investigations.

The adequacy of responses as measured by psychometric tests, was not predicted in most of the cases. The marked irritability, apparently poor judgment, alleged deterioration of intelligence, attention and memory, together with the behavior during emotional outbreaks, would lead one to suspect that the mental level, in many cases at least, was much lower than before the illness. This opinion was expressed, before the examinations, by parents, teachers, psychiatrists and psychologists. By psychologic tests, between the periods of emotional excitement when cooperation was good, all patients demonstrated an ability to give adequate responses. These responses compared well with the school record before illness as determined from personal interviews with teachers and school authorities in all doubtful cases. The patients were also able to pass school tests corresponding to their respective grades before the illness. Furthermore, reexaminations evidenced a normal rate of development of intelligence as shown by the stability of the intelligence quotients and a corresponding increase in material learned.

The emotional changes observed objectively, were often not proportional to the variations in the other mental capacities. These variations occurred during different examinations and in different parts of the same examination. Although showing polypnea and marked irritability, one patient, for example, gave adequate responses during a part of an examination. A varying amount of inhibition of associations and fluctuation of attention processes accompanied by affective changes was noted, however, in nearly all cases. This was evidenced chiefly by delayed or inaccurate response or prolonged reaction time. There was often difficulty in thinking for short periods suggestive of that seen in dementia praecox. Slight restlessness, wrinkling of the forehead and blushing were often the only objective evidences of affective change during the periods of greatest difficulty. It is quite probable that the increase in intelligence quotients on the second examinations of three subjects (Cases 5, 13 and 15) was due to affective changes which made response more difficult during the first examination. Cooperation was good and no emotional changes were observed during the time the examinations were being given. The extent to which these affective disturbances can be controlled, as well as many other questions, have not been answered in this study.

The memory tests used were for temporary retention and immediate recall. Specific tests for permanent retention were not given. There was no evidence of defective memory, however, from the psychiatric examinations and educational tests. Since "an intensive and uniform concentration of attention is the chief requisite for immediate retention," the memory for digits, sentences and passages gave good indices of attention. It must be remembered, however, that all the attention tests were for relatively short periods. It is quite probable that tests requiring longer periods of time would give variable results.

The average scatter in the Stanford-Binet intelligence tests was found to be four and one-tenth years. This is within the normal range, as determined by studies made at the Institute for Juvenile Research.

Attempts to educate many of these cases have not yielded efficacious results. The physical handicap, behavior difficulties and emotional outbreaks make it practically impossible to teach a large percentage of the children in the regular classes of public, parochial or private schools. The normal intelligence and absence of deterioration, on the other hand, demand that they be given an opportunity to gain an education and become economically independent. To accomplish this purpose training in a separate group by teachers who under-

stand the difficulties, seems most logical. In a large percentage of the cases this training can probably be best carried out under medical supervision.

DR. SIGMUND KRUMHOLZ: The paper brings out strikingly the fact that after lethargic encephalitis the patients may become affected in the emotional sphere without impairment of intellect. I have seen a few such cases, while other patients have both mental and emotional defect. Also, in some cases, the intellect has been really higher than it was before the illness. One of my patients, a man aged 29, presents a post-lethargic parkinsonian syndrome. Before the encephalitis he was an even-tempered man. Six months after the acute stage of the encephalitis he changed, became extremely irritable, and, in addition, has changed in his moral attitude and has become an exhibitionist. He exposes himself nude to women across from his apartment and masturbates. This he admits, but he states that he cannot help it even though he recognizes that it is wrong. His intellect, if anything, is above what it was before the illness. He is a cigar maker by trade and attempted to write stories before his illness though without success; since his illness he has written two scenarios, which were considered good but not sufficiently "snappy" for acceptance.

Another patient, a young girl, after an attack of lethargic encephalitis became extremely emotional, sentimental and intractable in school. The only thing she could be accused of was misbehavior; her intellect was not affected. She has good insight, but cannot control her emotions.

I think the paper is very important because we should recognize the fact that many patients, following lethargic encephalitis, may have defective emotion with normal intelligence. From the standpoint of mental hygiene we should recognize that fact, because the emotional upset is a question of readjustment and discipline, while on the other hand the intelligence defect is a question of special education.

DR. G. B. HASSIN: The most difficult and important phase in the encephalitis problem is the prognosis; that is to say whether the patient will get well completely or incompletely. As lethargic encephalitis is considered an inflammatory condition, a complete recovery might be expected. Yet a great many cases, among them those reported by Sherman and Beverly, show that recovery is too often incomplete. This is most likely due—as one case studied by me pathologically showed—to concomitant degenerative changes in the brain substance. The prognosis, therefore, in every case of epidemic encephalitis should be considered serious. If Dr. Sherman has an opportunity to supply us with pathologic material from some of his cases, histopathologic study would certainly be of great value and interest.

DR. LEWIS J. POLLOCK: I would like to ask whether there is evidence of recently acquired knowledge in these children, whatever the source.

DR. A. B. YUDELSON: In the study of post-encephalitic cases, some distinction should be made between encephalitis before and after adolescence. Juvenile patients are growing and developing individuals, who are constantly acquiring impressions. The disease may have destroyed many brain cells, but in the process of growth the unaffected brain, through reeducation, compensates for the loss. On the other hand, in adults who have reached full growth, reeducation is slower and more difficult. Whatever deterioration results from the disease, is not overcome by growth, as is the case in juvenile patients. In twenty postencephalitic persons in whom emotional instability is marked, no memory defect is apparent. But there is a characteristic slowness or mental rigidity,

comparable to the physical rigidity. It is difficult to say whether it takes long for these patients to get a thought or whether, because of their slowness in action, one only gets that impression. In some cases retention is poor. Hence, when the patient is told to do a certain thing and, execution being slow, a considerable space of time elapses between the command and the execution of an act, it appears to the examiner that either the patient has forgotten what he was going to do, or did not comprehend the command in the first place.

It has been mentioned here that some patients, on account of emotional instability, acquire hypersexual tendencies. One of my patients, aged 28, who had lethargic encephalitis at Cook County Hospital three years ago, for the past two years, or since shortly after the acute onset, has been impotent. The hypersexuality reported in the series related by the essayist, may be due to the fact that they were all pubescent; the normal impulse was not controlled or repressed because of the emotional instability, which was due to the brain lesions.

DR. SHERMAN (closing): Our cases showed no marked variation from the normal in the acquisition of knowledge. Of the twenty patients, seven carried on the school work and passed their grades. Those who were excluded from school were excluded not because of inability to learn, but because of behavior difficulties.

We found no slowness in giving responses or executing commands, except in four patients who showed marked muscular rigidity. Furthermore, it is difficult to differentiate between delayed responses due to physical slowness and slowing up of the mental processes. Since the only cases showing slow responses were those with muscular rigidity, it is probable that the slowness of which Dr. Yudelson speaks is physical rather than mental.

Abstracts from Current Literature

CLINICAL AND ANATOMIC STUDIES OF APRAXIA. Rudolf Brun, Schweiz. Arch. f. Neurol. u. Psychiat. **9**:29 and 194, 1921, and **10**:185, 1922.

The controversy centering around apraxia continues despite twenty years of endeavor. At the present time two almost diametrically opposed views occupy the foreground; the one, championed by Liepmann, seems to be the favored one, while the other, defended by von Monakow, has not enjoyed so large a following. The material on which Brun's paper is largely based comprises twelve brains, for the most part completely sectioned serially, belonging to the Zürich Brain Anatomical Institute. These were from patients showing apraxia as well as from so-called negative cases with a corresponding localization of the lesion.

The literature on apraxia begins rather late. Griesinger first called attention to the fact that aphasics were often unable to touch a required portion of the body on command. Finkelnburg, 1870, attributed this error of movements to a disturbance of recognition and coined the term asymbolism; under this he included not only the inability to recognize symbols, but all gnostic disturbances which today are grouped under the term agnosia. The so-called sensory explanation of apraxia was accepted in principle by most writers. Meynert built up the conception of motor asymbolism, since these disturbances occurred in the motor field. Kussmaul, 1877, limited this to the inability to perform the more common activities of daily life, and called it apraxia. Kussmaul, however, still held the view that these disturbances were based on a misconception of objects, sounds, etc. While the sensory theory of apraxia predominated during the last years of the past century, Liepmann, 1900, came to the conclusion that apraxia represents a disturbance sui generis, dependent on a more or less complete severance of the sensomotorium from distant sensory areas. The important observation, however, did not escape Liepmann that his hemi-apraxic jurist could, under certain conditions, perform well practiced acts, such as using a spoon, buttoning and unbuttoning his clothes; this he attributed to a local automatism of the sensomotorium, brought about by a kind of "short circuit" of impulses passing from the sensory post-central gyrus to the motor anterior central gyrus, a phenomenon which he explains by assuming the presence of a subconscious kinetic memory in the sensomotorium.

In 1905, Liepmann came to the conclusion that in right-handed individuals the left hemisphere, by means of the corpus callosum, had a dominating influence on the right hemisphere. Meanwhile Pick, in a careful analysis of cases of dementia paralytica, arteriosclerosis, etc., showed that in diffuse brain lesions there not infrequently occur marked apraxic disturbances. This form of apraxia he differentiated from that of Liepmann through its bilateral appearance, and explained it on the basis of a dissociation of a higher order caused by a loss of the original intention and a side-tracking of the complex into other fields. This disturbance he called ideational apraxia.

According to Liepmann, the realization of every act must be preceded by a goal idea toward which the movement is to be directed; supplementing this

goal idea there must be concepts of each component part of the act. These, in their entirety, make up the so-called movement formula.

Liepmann divides apraxia into two types, the motor and the ideational. In the ideational form of apraxia the muscles faithfully accomplish a movement, but this proceeds from a false objective. In motor apraxia, on the other hand, the disturbance relates to limbs and is limited to the musculature of the arm, the face, speech, mimic movements; it may be detected by very simple movements, such as closing the hand or moving the finger. In ideational apraxia, the partial movements of the act remain intact, but instead of accomplishing the desired objective, a false one is realized; ideational apraxia is only a partial expression of a general ideational disturbance; motor apraxia, on the other hand, is a focal symptom resulting from a lesion of a certain sharply circumscribed portion of the brain.

The motor apraxia of Liepmann is today divided by most authors into two subgroups; one, a segmental myokinetic form (gliedkinetische), or cortical apraxia, and the other an ideokinetic form, ideomotor, or subcortical apraxia. Goldstein adds to this an amnestic apraxia in which the patient has forgotten in toto certain complicated forms of movement.

The so-called apraxia regions, lesions of which necessarily result in a permanent motor apraxia, according to Liepmann are the following:

1. Apraxic regions of the left hemisphere are: (a) the left parietal lobe, including the gyrus supramarginalis and upper parietal gyrus, deep lesions of which result in right-sided ideokinetic apraxia; (b) the left central area plus the foot of the first and second frontal convolutions, lesions of which can seriously disturb the deposited kinetic engrams, as a result of which an inconsequential right-sided paresis may be accompanied by a very severe bilateral apraxia. A very extensive lesion of these areas would therefore result in right-sided hemiplegia and, through the medium of the corpus callosum, a left-sided, or sympathetic dyspraxia.

2. Large lesions in the right parietal lobe would not be without influence on praxia of the left hand. Large left-sided parietal lesions bring about a mild left-sided, or sympathetic dyspraxia.

3. Lesions in the posterior parietal region including the angular gyrus and the posterior part of the second temporal convolution and the anterior occipital region, result in ideational apraxia, particularly when associated with an extensive general atrophy of the brain.

4. The frontal lobe has nothing to do with praxia, although large lesions may inhibit initiation of movement.

5. Section of the corpus callosum brings about dyspraxia of the left hand, the fibers causing this forming the middle segment of the corpus callosum.

6. Lesions in the left and right centrum semiovale, as a result of interruption of fibers from the left sensomotorium to the right side cause the left hand to be dyspraxic.

7. For the uniformly bilateral apraxia of the head and of the muscles of the face, lesions in the lower third of the left anterior central convolution and Broca's area are responsible.

Some writers, as Goldstein and Hartmann, look on the frontal lobes as the real center of apraxia. Von Monakow's views are quite different. He believes that the combinations of movements of daily life, the so-called "kinetic melodies," are built up by a vast number of component parts which arise

initially from the instinctive and quite simple reflex mechanisms of earliest childhood to which experience and practice add more and more complex combinations of movement. Praxia, therefore, represents a developmental process, beginning in earliest childhood, which has occupied many years, which become more or less automatic, and is dependent not only on the function of the entire cortex, but also on the numerous subcortical reflex mechanisms. According to his view a sensomotorium, in the sense of Liepmann, does not exist. Praxia is simply a common possession of the entire brain. The real physiologic stimuli through which different praxias are brought to expression, or ecphoria, are, not preliminary visualization of movement, but those stimuli under the influence of which the movement under consideration was originally learned. The visualization of movements really occupies a very limited field in the integration and succession of various kinetic figures since many of these developed instinctively before the dawn of consciousness. It is not the countless centers of movement that are disturbed in apraxia, but only the integration, or ecphoria, inasmuch as the same patient who at one time cannot carry out a given command can on another occasion carry on the same activity spontaneously, when this is called for instinctively.

Monakow differentiates six forms of apraxia which cannot be sharply differentiated from each other.

1. Unilateral motor apraxia, the initial onset being accompanied by paresis of the involved extremity. This is essentially the same as Liepmann's ideomotor apraxia. In its later phases the patient can again manipulate with the apraxic hand; however, many mistakes are made.

2. Unilateral sensory apraxia, often present with sensory aphasia and cheirokinetic agraphia. Hypesthesia, stereoagnosia, and disturbances of deep sensibility are responsible in a large measure for this type of apraxia which is characterized by abnormal slowness of movement, faulty accessory movements, interruption of movement, etc.

3. Bilateral motor apraxia. In a sense this is a corollary of motor aphasia and in severe cases is accompanied by amimia and complete asemia, so that not even the simplest movement can be imitated correctly, although more complicated movements may occasionally be produced spontaneously. This form corresponds to the kinetic segmental apraxia of other authors. This form of apraxia is usually brought about by large vascular lesions in the left parietal lobe or by tumors during the phase of increasing hydrocephalus. The sympathetic apraxia of the homolateral, usually left, hand in these cases depends on a commissural diaschisis through involvement of the callosal fibers. Often a certain degree of general diorientation is present.

4. The agnostic form, or parapraxia. Here there is no hemiplegia, no disorientation; on the other hand, often sensory aphasia and optic agnosia. It is always bilateral. Simple movements are technically correct; however, in complicated movements there are numerous errors, misplacement of groups of movements, perseveration, and interruption, somewhat resembling the paraphasia of so-called transcortical aphasia. There appears to be an agnostic basis for this disturbance, a failure of the finer regulating control through the senses.

5. Amnestic apraxia. A pure disturbance of ecphoria analagous to amnestic aphasia.

6. Ideogenic form, corresponding to ideatory apraxia of other authors.

As to localization of apraxia, v. Monakow has reached the following conclusions:

Apraxia is in essence a temporary symptom complex, an answer of the entire central nervous system to a massive regional or general insult. It is practically never pure, but always associated with other coarse or finer disturbances of central innervation, such as paresis, aphasia, agnosia. In those cases in which the apraxia remains stable, enormous, deep or multiple lesions, associated with some chronic process and considerable circulatory disturbance, as arteriosclerosis or rapidly growing tumors are, as a rule, at fault. There is usually a protracted diaschisis. Apraxia, therefore, really belongs to the general brain symptoms which may, however, receive a peculiar local coloring because of the particular location of the lesion. The localities of predilection or "apraxia regions," are located in the entire territory supplied by the sylvian artery, particularly of the left hemisphere. Apraxia from lesions in the anterior part of this territory takes on the character of a unilateral motor apraxia; from lesions in the posterior part, particularly in the region of the second parietal and temporal convolutions, it has a bilateral character, associated with agnostic disturbances and sensory aphasia.

Writers, in criticizing Monakow's doctrine of diaschisis, explain this as a temporary phenomenon corrected by vicarious functioning. Monakow has repeatedly seen marked apraxia resulting from lesions of the brain which do not correspond to the apraxia regions of Liepmann, and on the other hand, in spite of a classical location, apraxic disturbances may be entirely lacking. The building up of an apraxia theory on the clinical basis of tumors is very treacherous, inasmuch as direct and indirect hydrocephalic pressure and distant symptoms cannot be evaluated properly. Any tumor, in any location of the brain, may result in apraxia.

In presenting his cases, Brun takes up first the vascular, traumatic, and encephalitic lesions, beginning with those involving chiefly the left parietal lobe.

Case 1. A cardiopathic man, aged 50, suffered apoplectiform insults of increasing severity in June and August, 1895, and in April, 1896. Following the first attack there was mild sensory aphasia, right-sided hyperesthesia with disturbance of deep sensibility, severe but transitory right-sided apraxia, and agraphia, followed by almost complete restitution, the patient being able to return to work. After the second attack there was a return of the aphasia, apraxia, and agraphia on the right side, word deafness, and alexia. Again marked improvement of apraxia and agraphia. With the third attack, which began with jacksonian seizures, the patient again became very apraxic, and this time bilaterally so. The sensory aphasia remained unchanged, the right hand permanently hyperesthetic and more or less apraxic, although the patient was able to do some work and write. He died after nineteen years from myocardial weakness. The patient could not follow the finger on command; however, he looked in the corresponding direction when a noise was made by snapping the fingers. At necropsy a very large vascular lesion was found in the left parieto-occipital lobe including the posterior half of the first temporal convolution, the middle third of the posterior central gyrus, and the lower third of the anterior central gyrus. There was general perivascular sclerosis and left internal hydrocephalus. Clinically this patient showed repeated right-sided apraxia of Monakow's sensory type with faciolingual apraxia, and marked recovery following each attack; after the third attack ideogenic parapraxic

disturbances predominated with sensory aphasia, right hyperesthesia and cheirokinesthetic agraphia.

A noteworthy observation in this case was that the initially very marked apraxic disturbances receded following each attack, although a massive lesion persisted. It could not be said that this patient's improvement was to be explained on the basis of vicarious function and reeducation inasmuch as the improvement each time was too rapid. Following the third attack there was a sympathetic apraxia in the left hand as well as a very distinct admixture of ideogenic apraxia as shown by the perseveration and mistaken movements. This case falls under Monakow's unilateral sensory apraxia. Another very important point was that this patient who could not raise his right arm to his head when commanded to do so, on leaving the physician shook hands with him quite spontaneously, under impulse of his natural affect. This was also shown when the patient was unable to go through the movements of eating when there was no food, while he did this with perfect ease when food was actually placed on the plate. In spite of the classic location of this lesion, severe apraxic disturbances were present only at the time of insult, followed by recovery sufficient to enable the patient to continue his daily work, and this in spite of the fact that we were dealing with a chronic progressive arteriosclerotic process.

Case 2. A traveling salesman, born in 1845, lost consciousness with the onset of a right hemiplegia, followed by complete, total aphasia, disorientation, and awkardness of the right hand in eating. There were repeated attacks followed by right-sided motor apraxia with ideatory and agnostic admixture followed by marked improvement each time. There was agraphia, right-sided hemianopia, hemiparesis, and hemihypesthesia. Anatomically there was found a vascular atrophy of almost the entire left parieto-occipital lobe, particularly the second parietal gyrus, also partial atrophy on the right.

Case 3. A right handed woman, 48 years of age, in 1905 developed vertigo, vomiting, left-sided paresis, and motor aphasia. Two months later there was a second attack with left sided hemiparesis, sensory aphasia, paraphasia, and agraphia. The right-sided apraxia disappeared completely. Anatomically there was found a softening of the right lower parietal lobe including the gyri supramarginalis and angularis.

In this case, although there was an area of marked softening in the typical location in the lower parietal lobe, with an otherwise perfectly normal brain, no permanent apraxic disturbance remained.

Case 4. This was a soldier, aged 24, who had a bullet wound of the left supramarginal gyrus but without apraxia.

Case 5. A boy, aged 9, who, following measles at six and scarlet fever at seven, developed epileptiform seizures of a jacksonian type with a progressive right-sided hemiparesis, including the arm, leg, and face; later there developed aphasia, but no apraxia. At necropsy an encephalitic lesion in the left precentral and central region with a traumatic hemorrhage in the left lower parietal lobe was found.

Case 6. A boy, aged 6, who suffered a fracture of the skull in the left parietal region in falling off a wagon. There was right hypesthesia with marked disturbance of deep sensibility and stereognosis, no hemiplegia, however, slowness of initial movements. At the onset there was bilateral apraxia which disappeared completely. In all probability this lesion was located in the left central parietal region.

Of the last three cases it may be commented that in spite of more or less extensive disturbance of the left parietal region in young patients no stable apraxia appeared.

The second group of cases had lesions located in the right parietal lobe.

CASE 7. A postmoster, aged 56, for sixteen years complained of headaches, for one year of vomiting, an epileptiform seizure with loss of consciousness, six months later a second epileptiform attack followed by an inability to read and a few months later, after a splitting headache, transitory blindness, left hemiplegia, and hemianesthesia. There was marked bilateral apraxia of the agnostic form with a faciolingual apraxia, visual agnosia, and disturbance of deep sensibility on the left side. Anatomically there was found a massive hemorrhage in the right parieto-occipital lobe and two smaller lesions in the left temporal lobe.

In this patient there was no definite improvement, which agrees with v. Monakow's contention that severe apraxic disturbances, remaining stable until death, signify either multiple lesions or a diseased brain.

CASE 8. A salesman, aged 68, suffered an apoplectiform attack with slowly progressing left sided hemiplegia and some disorientation. There was left hemianopia with a suggestion of visual agnosia, left paresis, ataxia, astereognosis, disturbance of deep sensibility, and mild bilateral apraxic disturbances, particularly of the left hand. This patient probably had a vascular lesion in the right parieto-occipital lobe.

CASE 9. A man, aged 36, right handed, at the age of 7 suffered a fracture of the skull from a fall. From the eleventh year of age he had epileptiform attacks. There was left-sided hemianopia and universal athetosis, particularly on the left. There was never apraxia. A traumatic cyst in the right parieto-occipital and temporal lobes was found.

This case supports v. Monakow's contention that in young individuals a large parietal lesion need not cause apraxia, and if so, rarely leaves a residual apraxia.

Lesions with predominant involvement in the left central area.

CASE 10. A shoemaker, aged 65, developed a right-sided hemiplegia, transitory, followed by alexia and literal agraphia. One month later he had an attack with motor aphasia. Three years later he was seen because of gangrene of the feet. The agraphia and alexia continued as before, but without history of an additional stroke there was added to it some apraxia. A vascular lesion in the left precentral and central area was found.

This patient had marked arteriosclerosis with diffuse involvement of all vessels of the brain and areas of softening in both hemispheres, particularly the left anterior central gyrus. The apraxic disturbances appeared only shortly antemortem with a progressive circulatory disturbance.

CASE 11. A waiter, aged 50, alcoholic, developed a right hemiplegia with motor aphasia, apraxia of the left arm, and faciolingual apraxia. On being told to close his eyes, he made an additional movement with his cane which was the result of perseveration, as he had made this movement with his cane just previously. Asked to show his tongue, he said "a" without showing his tongue, again an evidence of perseveration. Asked to blow away a piece of paper, he addressed the paper repeatedly by the word "one"; approached the paper with his mouth but did not blow it away. Instead of putting his hand on his head, he raised the arm vertically; instead of whistling, he opened and closed his mouth. He gave his hand, but when asked to hand his cane, held

it vertically upward. Asked to close a book he did so, but could not open it. Asked to close his eyes and make a threatening movement with his finger, he made some awkward movement. Asked to put the left finger to the right ear, he put his thumb into his mouth. In trying to light a candle, he took a match out of the box and rubbed it against the candle; some time later he lighted the match, but blew it out before the candle was lighted, probably the result of having anticipated this action. Asked to put his left hand on his head he could not do so, but when his head was suddenly tickled unexpectedly, he raised his left hand to the tickled spot reflexly and with perfect orientation on his own body. Asked to put the left hand to the right ear he could not do so, but when the ear was pinched unexpectedly he suddenly raised his left hand and threw the examiner's hand aside. Symbolic movements were poorly made on command; asked to make a cross he could not do so; however, on entering the church he crossed himself promptly and without hesitation. Ordinary movements, such as wiping up an imaginary spot could not be done; however, he immediately wiped up an ink spot, apparently made by accident. He could not repeat this movement when asked to imagine that the ink spot was again there. He dressed and undressed readily, but could not comb his hair when especially requested to do so. Spontaneous movements which accompanied his affective and spontaneous expressions were not normal, but somewhat uncouth and awkward. This is a disturbance which v. Monakow has termed parapantomimie.

It is to be emphasized in this case that the patient was able to carry out very complicated activities of daily life when the actual environment was present, but could not do this on request. Certain simple movements such as opening a book, when there was no apparent object in doing so, could not be performed; however, when asked to show a certain picture in the book the patient readily opened it. Whenever a natural impulse inaugurated the movements, these could be performed readily; thus, while the patient was unable to follow a finger with his eyes upward, he suddenly looked up when a five franc piece was held in the upper part of his field of vision. The question of simplicity or complexity of the act itself, therefore, is not so much concerned in apraxia. However, of utmost importance is the presence of an instinctive incentive in reality, appearing spontaneously. There was a rather prominent and lasting motor asymbolism and parapantomime. This is probably due to the fact that mimic and symbolism are to be separated in principle from praxia; they belong not to praxia, but to utterances of speech in a wider sense and are evidences of asemia.

Case 12. A boy, aged 7, injured the left frontotemporal area by sliding into a telegraph pole, following which he was unconscious for seven days, and developed a right hemiplegia and aphasia. At first there was a so-called sympathetic apraxia of the left arm which disappeared entirely in two months. A traumatic hemorrhage was found in the left central parietal area and Broca's region.

The following cases of tumor were cited:

Case 13. A bank teller, aged 58, developed a carcinoma of the thyroid, and soon thereafter headache and vomiting; he showed severe disturbance of deep sensibility and right astereognosis, paraphasia, marked bilateral apraxia (agnostic ideatory form), later word deafness, paresis, and general disorientation. At necropsy there was found a metastatic carcinoma, the size of a hen's egg in the medullary portion of the left lower parietal lobe in the region of the

supramarginal and angular gyri. In this patient the apraxic disturbances were from the start bilateral and accompanied by marked perserveration, bearing the stamp of a general dissociation of a higher order.

CASE 14. A notary, aged 37, developed headaches, general weakness, irritability, some disorientation, vomiting, disturbance of deep sensibility on the left side, left hemianopia, left sensory apraxia, with a suggestion of bilateral agnostic apraxia, and disorientation of time and place. Anatomically there was found a diffuse glioma deep in the medullary portion of the right parietal lobe, posterior half of the callosum, and penetrating into the left parietal lobe.

In spite of a large glioma involving the right parietal lobe and the posterior third of the corpus callosum, the apraxic disturbances appeared only fourteen days before death and were not very marked, being of a sensory character and largely limited to the left side. Here the agnostic character bilaterally present could easily be explained from a general disturbance of the brain as suggested further by slight dementia and disorientation.

CASE 15. A locomotive engineer, 52 years of age, developed hemiplegia, hypesthesia, marked disturbance of deep sensibility, and astereognosis on the left, and diminution of stereognosis, literal agraphia, and right motor ataxia on the right. Anatomically, a diffuse glioma was found in the medullary substance of the right parietal lobe, chiefly in the posterior portion with extension into the splenium which it destroyed completely. Here too, the apraxia appeared late and took on the character of a motor disturbance.

CASE 16. A moulder, aged 25, was knocked unconscious by a fall at the age of 5 years, following which he had petit mal attacks which gradually disappeared at the age of 14. He gave one the impression of being feebleminded. Only during a brief antemortem period in the hydrocephalic stage was there severe bilateral ataxia, which became submerged in the picture of general collapse with complete asemia and paralysis.

CASE 17. A woman, 59 years of age, began having headaches ten years previously; two months prior to death these became very severe and were accompanied by attacks of dizziness and vomiting. Shortly before death there was a marked diminution of spontaneous activity, later complete astasia and abasia, but no true apraxia. A glioma the size of a pigeon's egg had destroyed the genu of the corpus callosum, extending into the frontal lobe on the left and into the gyrus cinguli on the right.

The two last observations are of interest as the theory of apraxia applies to the frontal lobe. In the first case there was a short phase of bilateral apraxia which corresponded to the accumulation of spinal fluid within the ventricles. This soon disappeared, however, in the picture of general disintegration. In the second case a true apraxia was not noted so that this case can be considered negative as it applies to apraxia. There was, however, in both cases, a progressive diminution of spontaneous movement of all extremities which ended in a complete absence of spontaneous movement, giving one the impression that a progressively stronger impulse was required to bring about movement, as Hartmann and others have shown in similar cases of frontal lobe tumor.

CASE 18. A teacher, 47 years of age, suffered from a slight apoplectiform stroke with right hemiparesis. There was slight sensory aphasia, marked agraphia, later complete word deafness, severe bilateral apraxia with parapraxia (agnostic and ideogenic form) but no sensory disturbance. At necropsy a solitary tubercle, the size of a pigeon's egg, was found at the base, extending

into the left peduncle and into the subthalamic region and striate body. There was an enormous zone of vascular reaction.

In this case the subcortically located tumor had brought about a severe bilateral apraxia of a semic (agnostic ideatory) type. The case illustrates the fact that a localized lesion, without any involvement of the parietal lobe at all, can bring about a very marked apraxia.

Case 19. A school teacher, aged 50, who had had an amputation of the left breast because of carcinoma a year previously, developed headache in the region of the left frontal bone with fatigue, uncertainty in gait, vomiting, neuralgiform pains in the left arm, and, two months before death, an ataxia of the left hand, paresis of the masticatory muscles, marked bilateral motor apraxia, diminution of spontaneous initiative movement, and apraxic agraphia, with complete retention of isolated movements. The examination revealed multiple carcinomatous metastases in both hemispheres, varying in size from a hazel nut to a walnut, which were located in the caudal half of the thalamus, the central gyri, the first frontal, the first parietal, and the medullary portion of the supramarginal gyri on the left, and deep in the parietal lobe on the right.

Case 20. A woman, 48 years of age, two years after an operation for a carcinoma of the breast, became depressed, generally weak, suffered a light apoplectiform attack without paralysis or headache, and two months before death a subcortical sensory aphasia which progressed to word deafness, alexia, inability to understand sounds, right paresis, and apraxia of the left hand. Multiple carcinomatous metastases were found scattered through both hemispheres. Nodules were present in the leg region of the right anterior central gyrus, the right first parietal gyrus, the medullary substance of the left parietal lobe, and smaller ones in both occipital and frontal lobes.

Of the preceding twenty cases there were sixteen so-called positive cases in which more or less severe apraxic disturbances were noted, at least temporarily. In no case could the apraxia be considered as clear-cut or isolated. More or less severe cerebral disturbances, such as hemiplegia, sensory disturbances, agraphia, aphasia, or general psychic disturbances were present in addition. In nine of the sixteen positive cases there was hemiplegia and in four of these a so-called sympathetic apraxia. In motor apraxia it is almost a rule that, at least at the onset, there is a homolateral or a heterolateral hemiparesis; the sensory and agnostic-ideatory types of apraxia seldom develop with hemiparetic disturbances. In other words, when apraxic disturbances appear with hemiparesis, either on the same or on the opposite side, these almost invariably partake of the character of a motor apraxia. In three of the cases there was a left-sided hemiparesis, in two of which a typical right-sided sympathetic motor apraxia was present.

Of the sensory disturbances it may be said that a more or less marked diminution in cortical sensibility is often present in apraxia; when this sensory disturbance involves proprioceptive registration, that is, deep sensibility and stereognosis, the apraxia is usually of the sensory type.

When motor aphasia is present, the apraxia is predominantly motor; when sensory aphasia is present the apraxia is usually of the sensory and agnostic-ideogenic type. Liepmann, Pick, and Heilbronner regard aphasia as a motor apraxia of the speech musculature. This is probably true for the initial phase of motor aphasia, when not even simple sounds can be repeated, and one gets the impression that the involved kinetic synergies cannot be produced (ekphoriert) by the patient. Here motor aphasia impresses one as a partial expression of faciolingual apraxia. It is to be noted, however, that a very

severe motor aphasia may occur isolated and without any apraxia whatever of the face or hands. As far as sensory aphasia is concerned it may more consistently be considered to be akin to sensory apraxia, inasmuch as this form of apraxic disturbance seems to be dependent on a failure of proper proprioceptive orientation. The so-called jargon speech observed in paraphasia certainly suggests the parapraxic derailment of sensory and agnostic apraxia. Inasmuch as sensory aphasia, just as motor aphasia, may be present without accompanying apraxic disturbances, it would seem that this may be explained by the fact that the physiologic speech mechanism, both receptive, or sensory, and expressive, or motor, represents a more recent accomplishment from the phylogenetic and ontogenetic standpoints, and accordingly follows the law of integration, and is more easily disturbed than the other types of praxias. Apraxia may be present with optic agnosia. Liepmann at first repeatedly stated that optic agnosia does not exist with apraxia.

In the patients with psychic disturbances, the apraxia was usually bilateral and of the agnostic-ideatory type. The psyche is probably always involved to some extent in bilateral ideatory apraxia. In cases with agraphia, a disturbance of muscle sensibility and tactile agnosia may be present, for which the writer proposes a term "cheirokinesthetic," or "sensory agraphia." Agraphic disturbances may resemble apraxic disturbances, and we have here, just as we have there, disturbances of entire kinetic melodies (paragraphia) and of deficient initiation (amnestic agraphia). That agraphic disturbances occur so often in apraxia is probably also dependent on the circumstances that movements of writing, even more so than those of speaking, represent ontogenetically late acquisitions and are therefore easily vulnerable. For this reason also the restitution of agraphia is slower than is that of other apraxic disturbances; furthermore, it not infrequently exists as an isolated phenomenon.

In none of the sixteen positive observations did apraxia represent a stable symptom complex in the sense of a sharply circumscribed syndrome; it also underwent marked changes from time to time. In the initial, or shock period, or in tumors in the terminal state, all successively related acts were disturbed to some degree on one or both sides of the body. What was most noticeable in these cases was a general impediment in movement, or apathetic anastole, in the sense that the apraxic limbs could not be used without hesitation either on command or in the performance of spontaneous movements. This was particularly noticeable in frontal lobe tumors in which this disturbance may be so marked that the patient scarcely moves at all spontaneously, does not speak, expresses no wishes, and lies in bed completely akinetic. Kleist terms this phenomenon "psychomotor apraxia." Liepmann denies the relation of this to apraxia.

Faciolingual apraxia is only a partial expression of apraxia and is always bilateral. These patients cannot show the tongue, open the eyes, look to the right or left, upward or downward, on command. It was noted particularly in patients who had large lesions in the left lower precentral and central area. Whether the frequently observed conjugate paralysis is to be considered a transitory partial faciolingual apraxia is not certain. Faciolingual apraxia does not invariably require a left-sided lesion as Mingazzini maintains, nor a lesion in the precentral and central gyri; in Case 7 a large lesion in the right parieto-occipital area was found. Mimic expressions are to be differentiated from faciolingual apraxia and may be considered under the head of "mimic apraxia." It is true that they are often associated, but faciolingual apraxia usully outlasts the other. It probably was no coincidence that mimic apraxia

occurred in two cases of motor aphasia and suggests that we are dealing here with a disturbance of expression relating to aphasia in a broader sense.

In the initial stage of apraxia a fairly common, but, as a rule, transitory phenomenon is a disturbance of reflex localization movements of orientation on the own body. The patient cannot point to different portions of the body on command; he either does not react at all, or else makes an entirely different movement. Von Monakow reports a case in which one of his patients bit his own finger when this was put into his mouth. In all probability agnostic, or general semic disturbances were present. A more infrequent disturbance than faulty reflex pointing is the inability to point out and reach for objects which are to be selected. In none of these patients was this clearly present.

A very important point to which these observations call attention is the fact that the same patients who, under circumstances, can readily carry out very complicated movements, for instance, those concerning their daily life, provided these movements begin of their own spontaneous initiative, may be utterly unable to perform even the simplest acts when these are to be done contre coeur on command and when the real objective is not apparent. One patient, for instance, could not give his hand when commanded to do so, but, immediately after, on bidding good-bye gave his hand quite spontaneously.

All of these observations point to the fundamental fact that natural, spontaneous, instinctive activity comes by habit which aids in the ecphoria of movements. This is readily understood when the biologic laws of instinctive life are considered.

The instincts of self-preservation, such as defense and obtaining nourishment, are phylogenetically the oldest and best established heritage of the entire nervous system, indeed, probably of every cell in the organism; therefore it is not probable that they are bound to definitely localized regions of the cortex, but rather to the subcortical apparatus of the brain, spinal cord, and ganglion system as a whole. The primary ecphoria of the urinary instinct, for example, followed on the basis of an internal stimulus; this is true of hunger, thirst, pain, fear, libidinous impulses, etc., which are bound to specific visceral reflexes. These primitive impulses demand satisfaction and set into activity the entire cerebrospinal orientation apparatus as it applies to the outer world. If irritation complexes arise from the surroundings which satisfy these ancient hereditary impulses, then a mnemic homophony is established which expresses itself subjectively as a pleasant tension, or "klisis." Opposed to this is displeasure, flight, etc., which v. Monakow terms "ekklisis." The cerebrospinal motor apparatus is each time set into operation; the entire experience which caps and satisfies the original impulse, each time leaves behind it an engram complex which includes all the accompanying motor asynergies. Every repetition of the same or of a similar situation, gives rise to this same engram of experience complex. The ecphoria, which is accompanied by a subjectively lively affect, becomes more and more automatic with each repetition of the same motor synergies. Thus the original engram is enlarged with each succeeding experience and a broadened engram layer each time superimposed; the successive automatization and integration of these movement complexes, which become more and more complex, finally go to build up the engram strata and complicated praxias of each adult individual. As a consequence these automatic praxias of daily life become common property of a large associative territory of the entire nervous system and so cannot be permanently destroyed by a localized lesion. While the automatic action of these praxias may be disturbed, this limitation involves chiefly their ecphoria; that is, they cannot be awakened

in so many ways as formerly. This is particularly true of the purely mnemic impulses. So it is that patients cannot initiate various synergies on simple command. This is ontogenetically a recent acquisition of ecphoria, and as such is the first to disintegrate. Apraxia is not governed by simplicity of movement, but rather by its ontogenetic history. From the biologic standpoint there is a vast difference whether an accomplishment learned in early childhood—for instance, eating—is exercised under normal situation and affect with the actual meal before one, or whether it is done merely on command, from memory, and from an empty or imaginary platter. In the first instance all the instinctive and original moments under the mighty, driving influence of which the activity was first learned and practiced are present, and as a result this ecphoria still remains possible in the face of the severely damaged brain of the apraxic patient, as soon as this has recovered from the accompanying diaschisis; in the second case there is only the stimulus supplied from memory, which is inadequate and under which the defective brain gives way, and the performance of the desired movement becomes impossible.

Summarizing: Every repetition of a kinetic melody leaves behind it a new engram complex which is superimposed on the early deposited experiences, to which it becomes attached, and to which new sensory and motor details are added; a constantly enlarging field of activity is thus developed. The zone which may bring about the ecphoria of complexes gradually becomes larger and larger, that is, after so many thousands of repetitions it can be excited from every part of the brain. It is just the reverse of Mingazzini's contention that the automatization of praxia depends on a gradually shrinking and sharper localization in the cortex of the corresponding engram complex; on the other hand, it results from a constantly enlarging field of irritation which permits the inauguration of certain movements more easily and from more widely separated portions of the brain.

Liepmann distinguishes two forms of apraxia, motor and ideatory. The motor apraxia he divides into a limb-kinetic apraxia and an ideokinetic apraxia; the former is essentially identical with the cortical apraxia of Kleist and Heilbronner, the latter with the subcortical apraxia of Heilbronner. Brun believes that these separate forms cannot stand independently and would suggest the following classification which must not be regarded as being drawn along hard and fast lines, inasmuch as the expression of the apraxia may change rapidly from time to time.

A. Unilateral apraxia. 1. Unilateral motor apraxia, present with crossed hemiplegia and motor agraphia, often with initial paresis of the subsequently apraxic hand and frequently associated with motor, less often with sensory aphasia. No sensory disturbance in the apraxic extremities. 2. Unilateral sensory apraxia. The apraxic disturbance seems to be caused by a severe homolateral disturbance of proprioceptive sensation (bathyanesthesia and tactile agnosia) and is often associated with severe cheirokinesthetic agraphia and with sensory aphasia.

B. Bilateral apraxia. 1. Bilateral motor apraxia as under A 1, only bilateral and with more prominent agnostic and ideatory elements. 2. Bilateral agnostic-ideatory apraxia. These forms cannot be separated clearly: (a) Agnostic apraxia. The agnosia is prominent; (b) Ideatory apraxia. The ideatory, or psychic disturbances are prominent; (c) Amnestic apraxia. This classification agrees pretty closely with that of v. Monakow.

The clinical progress of apraxic patients varies. There was only one vascular case which showed a progressive disability as opposed to the seven cases of

tumor. General improvement is to be expected in those of vascular origin. Complete recovery was noted in three cases. The following rules may be laid down:

1. In traumatic lesions, when the balance of the brain is uninvolved, and particularly in youthful individuals, even a very severe initial apraxia will clear up.

2. In those cases in which apraxic disturbances remain stationary for months or years before death, usually multiple defects or severe general pathologic processes such as arteriosclerosis, hydrocephalus are present. Not infrequently, however, even under these conditions, marked improvement may occur in the early stages, when the onset is sudden, as in apoplectiform seizures.

3. A progressive course in the severity of the apraxia is seen almost only in tumors, rarely in vascular lesions under the unfavorable circumstances noted under 2.

4. Apraxia therefore is, in principle, a temporary symptom whose appearance can never be explained through the action of one localized lesion, regardless of its localization; invariably its initial appearance is accompanied by more or less severe general cerebral disturbances such as diaschisis.

While it has been emphasized that the appearance, and particularly the continuation of apraxia, is always accompanied by a general pathologic process it is not to be understood that local moments are without significance, and that there are not certain regions in the brain, lesions of which do not readily result in the production of apraxia. It was at once apparent that of the sixteen positive cases of apraxia, the lesion was present in the classical apraxia region, that is, the left lower parietal lobe, in only one instance. Furthermore, in contradistinction to this very scant support there were two patients who, in spite of lesions of the left gyrus supramarginalis, had no apraxia whatever. Conclusions with regard to localization may be drawn as follows:

1. There is no region in the brain a lesion of which may not result in apraxia at least temporarily.

2. Total disturbance of the left inferior parietal lobe alone does not necessarily result in apraxia.

3. The real apraxia region par excellence includes a very much larger territory, that is, de facto, the entire territory supplied by the posterior branch of the artery of the sylvian fissure. In order to bring about even initial apraxia, however, a large area of this region, which extends from the anterior central gyrus to the mid-occipital region and deep into the substance of the brain, must be destroyed. Even right-sided lesions of this territory in right-handed individuals may give rise to a severe homolateral apraxia. Usually, however, but not always, the apraxia takes on the character of an agnostic-ideatory type.

4. No special importance can be assigned to the frontal lobe as a center for praxia. When apraxia occurs in cases of this type, we are probably always dealing with distant symptoms of various kinds, such as hydrocephalus, diaschisis, indirect pressure, etc.

5. Even the peculiar inhibition of movement which is seen in some of these patients, cannot be regarded as a truly apraxic symptom and is probably due to diaschisis.

6. By the same token, the corpus callosum plays a similar rôle in the production of apraxia, since the latter concerns itself with the commissural conduction of the diaschisis and because of the predominant influence which the

left hemisphere exercises over the right, lesions located in the left hemispere more often result in a homolateral as well as a contralateral apraxia than do lesions located in the right. This so-called sympathetic dyspraxia of the left hand is accordingly no permanent symptom; it is in principle a temporary symptom, so far as the affected kinetic melodies, having been practiced bilaterally since earliest childhood, have the corresponding engram complexes deposited in both hemispheres. Furthermore, there is no ground for believing that involvement of the anterior part of the corpus callosum results in more disturbance than does involvement of the posterior part.

7. As far as the more localized lesions in the various subdivisions of the apraxia area are concerned, the following may be stated: (a) Unilateral motor apraxia is particularly evident in extensive lesions of the anterior portion of the apraxia region (left precentral, central, and parietal areas) and about equally common on the homolateral side as a so-called sympathetic apraxia, as on the contralateral side; (b) unilateral sensory apraxia is particularly apt to appear in involvement of the opposite lower parietal area and posterior portion of the first temporal gyrus; (c) bilateral agnostic-ideatory apraxia is noted most frequently in deep-seated disturbances of the posterior portion of the apraxia region (parieto-occipital lobes on either side); however, only with synchronous general disturbance of the brain. The apraxic condition takes on more and more of the agnostic character the farther backward the lesion is located.

8. A severe and permanent motor asymbolism and parapantomime result particularly from lesions seated deep in the head region of the left anterior central gyrus.

9. Faciolingual apraxia also appears especially from lesions of the corona radiata of the left anterior central gyrus in the head region; however, never as a permanent disorder but only as an initial symptom. This can be also present in large parietal and even in right-sided occipital lesions. The symptom has nothing to do directly with involvement of the frontal lobes.

10. In all cases in which apraxia becomes chronic, that is, when it becomes a stable syndrome, one is dealing either with enormous or multiple vascular lesions associated with severe general pathologic processes or with tumors with correspondingly severe secondary manifestations. That this is true, is shown by the observations of Pick who found typical apraxia in senile dementia, progressive paralysis, and after epileptiform attacks; by Westphal who noted it in post-traumatic dementia with general arteriosclerosis, and in carbon monoxid poisoning; by v. Monakow who described it in severe intoxications such as uremia.

In the development from the lower to the higher forms of life, the development of kinetic movements through practice begins coincidently with the development of the cerebrum. With the progressive growth of higher centers, the subcortical reflex apparatuses are robbed in part of their function, the higher mnemic activities being taken away. There appears to be a progressive wandering of these functions forward. In a new-born child the reflex mechanisms begin their work instinctively. Examples of this are the sucking instinct and protective instincts, such as crying, and kicking. Added to these reflexes, however, must come some control from the cerebrum, as shown in the faulty scratching reflexes of the spinal cat. In newly born children the reflexes shown are, likewise, often very ineffective. On the other hand, this reflex substructure furnishes the foundation for later praxias. One of the first additions to these

early reflexes is the function of orientation on the own body. This is done under the direction of sensitivity. The various orientation movements are then allied and coordinated; for instance, the movement of the hand to an irritated part may be accompanied by a conjugate movement of the eyes in the same direction. Later, expressional movements as crying and mimic are added, inasmuch as affect accompanies the particular reflex. Then follow the principal movements such as sitting up, standing, walking, running, jumping, climbing, swimming, and eating. Finally are added the finished movements, such as orientation on objects, which, in later life, become such a sovereign accomplishment. The successive acquisition of these complicated integrations and the learning and practice of the countless kinetic melodies of daily life continues constantly under the influence of higher instinct forms, particularly under the urge of consciousness. For instance, in learning to play the piano the first movements are extremely slow and awkward, but on repetition engram complexes are deposited which make these movements more and more easy and ultimately automatic, without appreciable psychic exertion, and without much conscious planning. If we were to consider the "how" of each individual movement we should never arrive at the goal: we should be in the position of the unfortunate centipede of the Indian fable who wondered just how it should move its legs in order to move; it considered this matter at such length that finally it was unable to get away at all. The same thing applies to the theory of some authors who believe that every movement we make must be preceded by a similar psychic preparation. Actually, the source of movements belongs to our early childhood. If this is true, then interference with such a complex mechanism cannot be accomplished permanently by a localized defect; this would require some injury of the entire brain, either through a diffuse pathologic process, through toxic influences, or through diaschisis. While a localized lesion can cause some interference with praxia it cannot permanently abolish it.

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POSITIONS OF THE HEAD AND MUSCLE TONE. A. SIMONS, Deutsch. Ztschr. f. d. ges. Neurol. u. Psychiat. **80**:499, 1923.

In this article of fifty pages the author considers the effect of various positions of the head on the associated movements of hemiplegia. It is, therefore, a clinical and practical application of part of the experimental work of Magnus and de Kleijn dealing with the influence of reflexes originating in the cervical muscles, the labyrinth and in midbrain centers, on positions of the torso and limbs.

Simons' work was begun, in 1919, on a case of hemiplegia resulting from a war wound and since has been carried out by observations on more than two hundred paralytics. Simons has found that associated movements occur less frequently in hemiplegics over fifty than in younger persons. He warns against examining the patients in cold places since this increases the contracture and may change entirely the type of reaction. Patients who are fatigued may show no effect of changes in head position on muscular formulas of the associated movement. The patient should be examined on a hard table rather than on a bed.

Simons states that movements of the head alone, no matter how carried out, will produce neither a visible nor palpable change in the tone of the extremities at rest. Movements of the head alone against resistance likewise produce no such changes. The influence of head movements was mani-

fested only when associated movements were produced in the paralyzed arm or leg by active innervation of some sort in the unparalyzed limbs. In some cases active innervation of the paralyzed limb produced associated movements in it which could not be produced by any form of active innervation of the unparalyzed limb.

Various positions of the head were used, namely, ventral or that in which the head was flexed forward, its opposite the dorsal, right and left lateral flexion, and rotation to the right or left. There is considerable variation in the changes that occur when the head is moved from one position to another according to the position in which the patient's head is at the time when active innervation initiates associated movements (Figs. 1 and 2). Simons gives a table showing the two different types of reaction that occur most commonly in the arm and leg. When the head is rotated toward the unaffected side there is:

(1) Increase of abductor tonus at the shoulder.

(2) Flexor tonus at the elbow.

(3) Almost always extension of the hand of equal intensity, though this is sometimes weaker than that obtained by turning the head to the affected side.

(4) Increase of flexor tonus at the hip and knee, and dorsiflexion and supination of the foot.

When the head is turned to the affected side there is:

(1) Increase of adductor tonus at the shoulder.

(2) Extensor tonus at the elbow.

(3) Often inward rotation of the arm.

(4) Almost always extension of the hand.

(5) Increase of extensor tonus at the hip and knee.

(6) Increase of adductor tonus at the hip.

(7) In some cases, internal rotation, dorsiflexion and supination of the foot; in others, plantar flexion.

When the head is bent forward, ventrad, there is most often increase of adductor and extensor tone. There may, however, be increase of flexor and abductor tone. When the head is in the dorsal position the opposite conditions obtain.

Another table is given showing that, at times, the *same* reaction occurs when *opposite* positions of the head are produced. Though some of these reactions are of equal intensity, that is to say, the angles produced are equal, in other groups the reaction is in the same direction, but the change in angle is not equal. Reactions are most conspicuous at the shoulder, elbow, hip and knee, while at the ankle and wrist, position reactions are not so common nor so easily made out. Reactions of the fingers and toes, dependent on changes in the position of the head, are very rare and uncertain. The amount of paralysis, contracture or remaining cortical sensation has no effect on the action of the head in influencing associated movements. Stimulation of the labyrinth has no effect. Increase of tone produced in the affected limb during the associated movement begins shortly after activation elsewhere has begun and continues usually until activation has ceased.

Simons then considers the portions of the brain which must be injured in order to produce associated movements and emphasizes the fact that some

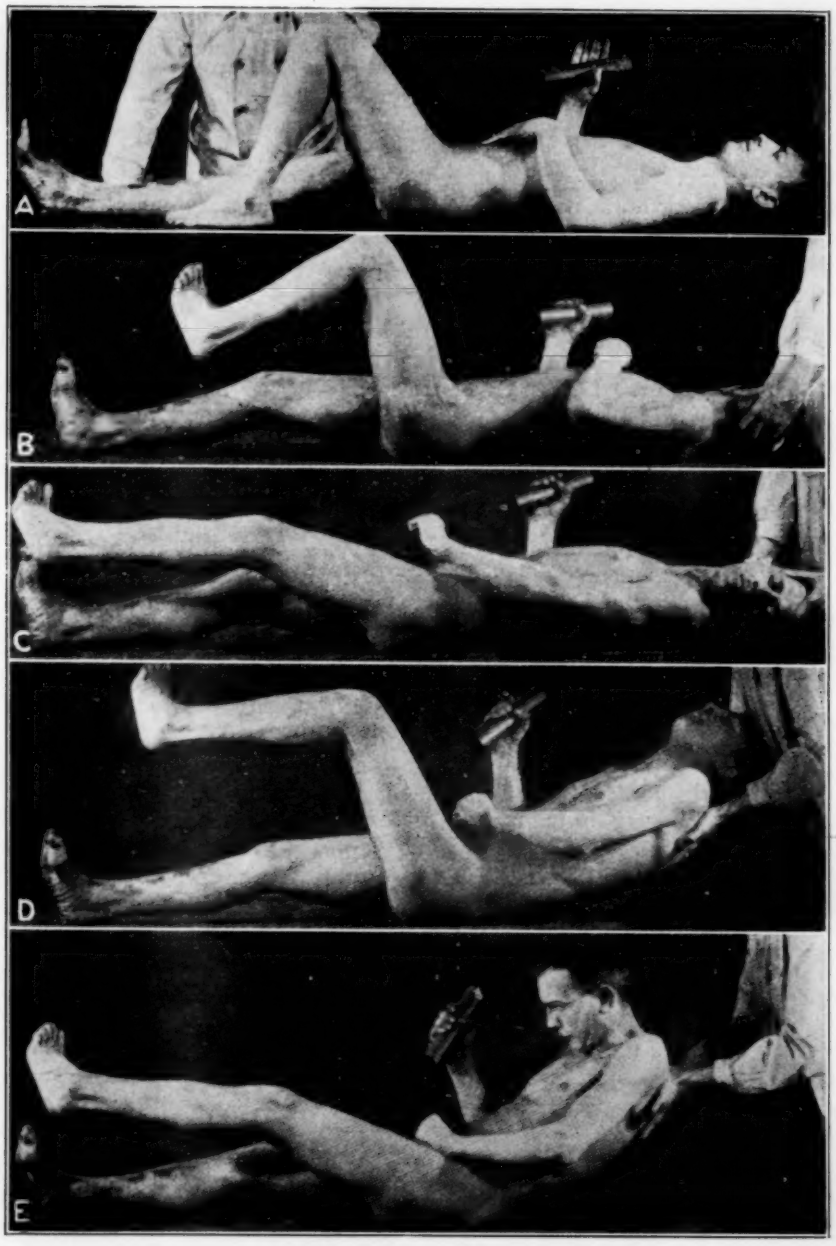

FIGURE 1

EXPLANATION OF FIGURE 1

Fig. 1.—Marked left-sided hemiplegia due to a gunshot injury to the brain.

A. Initial position. The right hand is holding an elastic cylinder loosely. The paretic left leg is held in the position shown in order to demonstrate the subsequent production of extensor tonus. The left leg, were it not held, would fall outward on account of paralysis. The investigator is holding the knee until tonus is initiated.

B. The head has been turned to the right. Marked hemiplegic associated movements have been produced by closing the fist forcibly about the elastic cylinder. The arm leaves the position of rest seen in *A* and shows abduction of the upper arm, marked flexion of the elbow, lifting of the hand and closing of the fist. The flexor tonus of the arm is extremely great. Simultaneous stretching of the triceps may be seen. In the leg there is mild inward rotation at the hip and marked flexion at the hip and knee. The flexor tonus is considerable in the knee as was demonstrated by passive extension. The foot is lifted, adducted and supinated; the toes are extended. The associated movement of the unaffected leg is readily seen.

C. The head has been turned to the left. The initial position was that seen in *A*. This shows contraction of the facial muscles, extension, abduction and mild inward rotation of the arm and flexion of the hand on closing of the fist. The hand is carried to the neighborhood of the symphysis. In the leg there is marked extension at the hip and knee with powerful internal rotation, dropping of the foot and extension of the toes. Simultaneous stretching of the biceps in the upper arm is not visible on account of lighting effects.

D. The head is pushed dorsad. Flexor tonus of the extremities is like that described in *B*.

E. The head is pushed ventrad. Extensor tonus of the extremities is as described in *C*. If motion pictures of these patients are taken from above it is seen that when there is flexor tonus of the extremities the adductors of the hip and shoulder are relaxed and, as a consequence, the arm and thigh are easily abducted and externally rotated. When there is extensor tonus, on the other hand, the adductors become much contracted when passive abduction is tried and it is not possible to abduct under these circumstances.

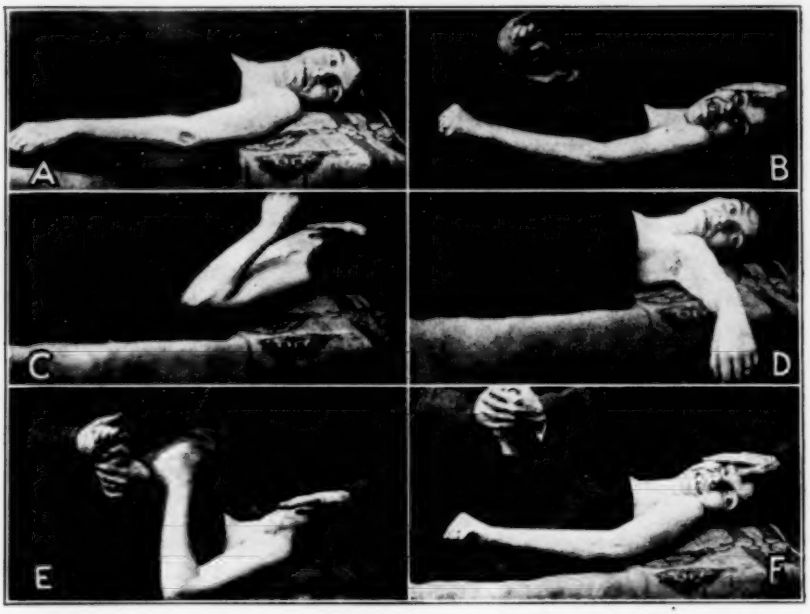

Fig. 2.—Left-sided hemiplegia due to an embolism of cardiac origin.

A. Initial position for *B* and *C*.

B. Production of hemiplegic associated movements by forcible clenching of the right fist. Very strong adductor and extensor tonus with lifting of the shoulder, slight pronation of the forearm; extension of the hand and closing of the fist. Facial paralysis is easily seen.

C. The head has been turned to the right. The torso conceals the right arm. The right hand is grasping a dynamometer. There is marked flexion at the elbow and supination of the forearm which could not be overcome by passive movement. There is ulnar abduction of the hand and closing of the fist. Adductor tonus of the shoulder muscles is not visibly altered, but, on palpation, is much weaker than that found in the position shown in *B*.

D. Initial position for *E* and *F*. Right angle horizontal abduction of the extended arm, dropped wrist.

E. The head has been turned to the right. Clenching of the right fist. There is adductor tonus of the upper arm which, however, can be easily overcome. There is flexion at the elbow to a right angle and supination. The hand and finger muscles show the positions previously described.

F. The head has been turned to the left. There is powerful clenching of the fist, and facial paralysis as above. Marked adduction of the upper arm which can scarcely be overcome by passive movement. The angular relations to the trunk are, however, the same as those seen in *B*. There is marked extension of the forearm with very slight flexion at the elbow.

involvement of the pyramidal tract must occur which releases the activity of physiologically lower centers. He also states that associated movements in conditions other than hemiplegia were extremely rare, that they never occurred when extrapyramidal syndromes alone were present, nor in cerebellar disease. That associated movements may depend solely on the activity of the spinal cord when isolated from prespinal centers by injury or disease, has been abundantly demonstrated.

Simons emphasizes the difference between labyrinthine and neck reflexes, which are demonstrated by the work of Magnus and de Kleijn. His paper deals with the latter group. The labyrinthine reflexes depend on the integrity of the eighth nerve and its continuations, while the neck reflexes are dependent on the integrity of afferent fibers from the cervical muscles. The head leads the body as is shown by the influence of positions of the head on positions of the trunk and extremities. Simons also points out that the neck reflexes are carried out by the spinal cord.

In hemiplegia it would appear that, when stimulation occurs, as by making a fist on the unaffected side, an impulse passes to the contralateral side and being uncontrolled by higher centers, probably the pyramidal tract, produces associated movements. Changes in head position, since they are capable of altering the positions of the extremities and trunk, that is, the more caudad portions of the body, will naturally alter the muscular formulas seen in the associated movements.

The muscular formulas of the associated movements as given by Simons are in many cases parallel to those obtained in decerebrated animals, in which opposite positions of the head produce opposite positions of the limbs. However, the formulas he describes are not always constant and, as might be expected, the precise results of animal experimentation are not always found in the less clearly cut conditions of human pathology.. Simons touches on other points of a more theoretic character and also gives an excellent review of the literature. The article is abundantly illustrated by good photographs taken from motion picture films, two of which are reproduced. The article is an important contribution to this aspect of motility disorders.

KRAUS, New York.

THE FINE STRUCTURE OF MEDULLARY SHEATHS OF NERVE FIBERS IN NORMAL AND PATHOLOGIC CONDITIONS, AND A SIMPLE STAINING METHOD FOR MYELIN SHEATHS. S. KAMIJO, J. Tokyo M. A. **37:** No. 7.

In researches on the finer structure of nerve fibers, it has generally been found that those methods involving imbedding in celloidin are unsatisfactory. This is largely due to the changes produced in the myelin by the agents, such as alcohol or ether, that must be used in this method, and the production of artefacts that make difficult an interpretation of what one sees.

The writer has developed a method of preparation that does not injure the myelin sheath and reveals its histologic structure in clearer details than has heretofore been possible.

The method is as follows:

1. Fix in 5 to 10 per cent. liquor formaldehydi (3 to 5 days).
2. Cut frozen sections (5 to 20 microns).

3. Stain in one of the following solutions for three hours in an incubator or more than six hours at room temperature.

(a) 10 per cent. alcoholic hematoxylin stock solution..... 20.0
Saturated solution of alum..... 100.0
Glycerin 100.0
Glacial acetic acid..... 3.0

This solution must be exposed to light until it develops a deep red color.

(b) Ripened solution of Böhmers hematoxylin..... 200.0
Glycerin 100.0
Glacial acetic acid..... 4.0

(c) Delafields hematoxylin.

(d) Ehrlich's hematoxylin (for brain and cord).

4. Rinse sections for a short time in water.

5. Differentiate in Weigert's borax-potassium ferricyanide solution, using various dilutions.

6. Wash thoroughly in water.

7. Dehydrate, clear and mount in balsam. If desired one may use various counter stains.

A summary of the results of studies on the medullary sheath in preparations according to these methods is as follows:

1. The medullary sheath shows a granuloreticular structure. In longitudinal sections of a nerve fiber one may see numerous granules with a network traversing among them. In alum-hematoxylin stains, the granules take a deep blue color while the network remains pale. In transverse sections the granules have a radial arrangement between the segments formed by the pale network.

2. The granuloreticular structure is best brought out in material that has been fixed in formaldehyd, especially when used in high dilutions. It may also be seen in material either unfixed or fixed in other solutions, but in these latter methods the details are very obscure.

3. The granules are soluble, in varying degrees, in either chloroform, acetone, alcohol, methyl-alcohol and iron alum solution.

4. The structural appearances described, readily undergo postmortem changes. The nerve fibers then stain faintly, the granules disappear, and the network disintegrates and stains a blue color. This disintegration is most pronounced in cases of putrefaction.

5. This granuloreticular structure has been demonstrated in the medullary sheaths of the following vertebrates: ox, pig, horse, guinea-pig, white rat, house rat, mouse, pheasant and frog. The distinctness of the structure varies in different animals. It is very well marked in the pig and guinea-pig, and less well defined in the rabbit and frog.

6. In young animals the granules are large and plump, giving little space to the intervening network, while in older animals the network is wider and the granules are considerably reduced in size.

7. The appearance of the structure seems to be influenced by the state of nutrition. In emaciated animals the granules appear very small and shriveled when compared with those of normal animals.

8. This characteristic structure is especially distinct in the trunk of the nerve fibers and less so in the proximal and distal parts where the sheath

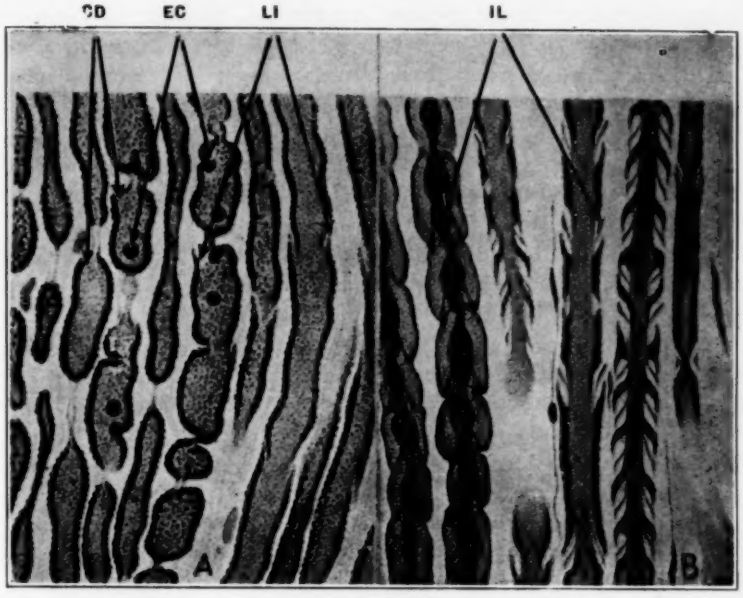

Fig. 1. A.—Longitudinal section of an ischiatic nerve of a white rat, showing granuloreticular structure, Lantermann's incision (LI) and cylindric degeneration (CD). Note that the cylindric degeneration appears in close relationship with the Lantermann's incision. The figure shows also the manner in which the globules (Elzholz's corpuscles, EC) make their appearance. (Acid glycerin-alum-haematoxylin staining).

B. Longitudinal section of an ischiatic nerve of a white rat; showing particularly well stained interlamella (IL) -(Alum-haematoxylin-carmin-staining).

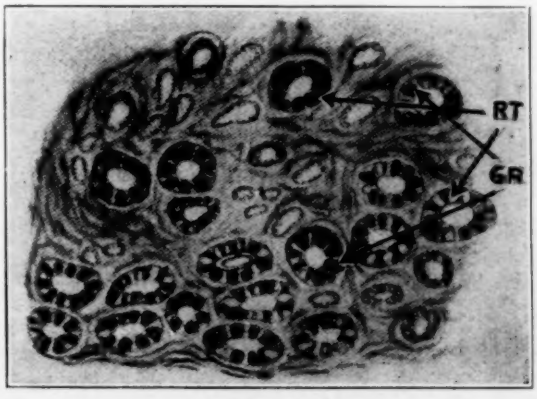

Fig. 2.—Transverse section of an ischiatic nerve of a white rat, showing radiary arrangement of reticulum (RT) and granules (GR).

diminishes in thickness. Traces of this structure can still be seen in the fibers of the spinal cord, but not in those of the cerebral cortex or in the nerves of the external integument.

9. If degeneration of nerve fibers proceeds beyond a certain degree, the details of this finer structure disappear.

10. As the granuloreticular structure can be regularly observed in normal medullary sheaths, and as the changes take place according to certain principles, it is reasonable to conclude that the structural differences between reticulum and granules existed during life.

11. The reticulum is identical with the Neurokeratingerüst of Ewald-Kuhne and Ernst's Radspeichenbau observed in transverse sections of medullary sheaths, and is not to be regarded as an independent constituent.

12. The so-called Lantermann's net seen in osmic acid preparations looks very much like our reticular portion and is probably identical with it, as it would not be likely that two such similar structures would exist in the same place.

13. Lantermann's incision has been clearly demonstrated in all medullated nerve fibers so far examined when fixed in dilute solutions of formaldehyd. The funnel consists of a peculiar structure which corresponds to the interlamella of Kuhnt. It stains with carmine, while the reticulum never takes this color. This can be well shown in preparations fixed in 4 per cent. liq. formaldehydi and stained in hematoxylin-carmine solution (one part lithium carmine and four parts glycerine-alum-hematoxylin).

14. The interlamella may serve in the penetration of nutritive material among the elements of the nerve.

15. The medullary sheath, being lipoid in nature, will maintain a cylindrical form from the balance sustained in its biologic functioning. If any one point of a neuron is damaged, this balance is lost and changes in the form of the sheath will occur in accordance with physical laws. This is a phenomenon of degeneration.

16. The degeneration of medullary sheaths may be divided into two categories:

(1) Cylindric degeneration.—This begins distal to the point of damage and occurs when the nerve fiber is injured and the axis cylinder is involved. The first sign of degeneration is the separation of the medullary sheath at the interlamella or Lantermann's incision, the fiber taking on a cylindrical form.

(2) Globular degeneration.—This occurs when the damage to the sheath is more superficial and a metabolic disturbance is produced. Globules then form inside or outside the sheath. These globules are identical with the so-called Elzholz corpuscles. These corpuscles may be found in sparse numbers in nerves that are quite normal and may be regarded as the effects of local disturbances in the metabolism of the nerve.

17. Wallerian degeneration is chiefly of the type of cylindric degeneration, globules appearing only in later stages, excepting in the neighborhood of the injury.

18. In neuritis caused by lead poisoning, globular degeneration plays a principal rôle, while cylindric decay can only be seen in advanced cases.

19. Degenerations produced by perineural injections of ether, chloroform, acetone, alcohol or oil of turpentine are of the globular type. If, however, the injury involves the axis cylinder, degeneration of the cylindric type will take place in the distal part.

20. The toxins of tetanus and diphtheria produce the globular type of degeneration.

21. In beri-beri, globular degeneration first appears and later is followed by cylindric degeneration according to the progress of the disease. In addition to this the granules atrophy, probably because of the nutritive disturbance.

KAMIJO, Tokyo, Japan.

REMARKS ON THE RECOVERY OF A CASE SHOWING THE BROWN-SEQUARD SYNDROME. PIERRE MARIE, H. BOUTTIER and RENE MATHIEU, Rev. neurol. **28**:976 (Sept.-Oct.) 1921.

The article discusses a case showing the Brown-Séquard syndrome in which there are marked differences from the five cases published by M. Goldflam in September, 1919. The patient is a diamond cutter, aged 53 years. The first symptoms occurred in October, 1919, and were marked by pain in the cervical region and the occiput which was perceived on movements of extension of the neck and head. Gradually there appeared, in about fifteen days, motor symptoms on the right side and sensory disturbances including various forms of superficial sensibility on the left; two months after the onset, the authors examined the patient and diagnosed the case as one of the typical Brown-Séquard type with the lesion at about the sixth cervical segment. Gradually the symptoms became more diffuse. About January, 1920, motor symptoms appeared on the left side also; there was practically a complete quadriplegia with bilateral pyramidal tract signs, diffuse pains, and objective sensory signs, characteristic of the Brown-Séquard syndrome. Spinal puncture showed no lymphocytosis, although there was a slight increase in the albumin. The spinal fluid Wassermann reaction was negative; radiographic studies of the cervical spinal vertebrae were also negative. Clinical examination of the spinal vertebrae was also negative for pain on pressure and for rigidity; there was no limitation of movements of the cervical spinal region, either active or passive.

The patient remained for many months in the same condition confined to bed. The question of diagnosis then arose, particularly as to whether the case was one of cord compression or myelitis. The question of operation had to be considered, but it seemed best to temporize. Gradually the motor symptoms became less severe and the sensory symptoms improved simultaneously. By July, 1920, the patient was able to walk, and a year later he was apparently as well as ever.

The authors regard the existence and duration of the quadriplegia as quite striking, and because of this, together with the other symptoms, regard it as an instance of the so-called, "benign form of the Brown-Séquard syndrome." In comparing their case with those reported by Goldflam, they note several likenesses and differences.

As for the similarities: first, the patient is 53 years old (all of Goldflam's cases fell between 30 and 50); second, all show the Brown-Séquard syndrome with the pyramidal tract symptoms in the paralyzed side; third, the residuals are slight and the etiology is unknown.

The differences between Goldflam's cases and the case under consideration are numerous; first, the onset in the present case was sudden; second, the Brown-Séquard symptomatology was very marked, diffuse and ended in a quadriplegia; third, the root pains were severe; fourth, the localization was in the cervical and not in the dorsal region of the cord; fifth, there was no sphincter or genital disturbance; sixth, the course of the case was quite rapid, all of the symptoms having practically disappeared at the end of eighteen months. The authors regard the differential diagnosis as very difficult. Syphilis is ruled out by the negative spinal fluid, absence of ocular symptoms, and recovery without treatment. One of the funicular myelitides might be considered, but the localization or segmental character of the lesion is against this conclusion. Medullary compression is favored because of the root pains, the sensory disturbances, the Brown-Séquard syndrome, dissociation of the radial and cubital reflexes, motor and pyramidal symptoms, etc.; but the nature of the compression would be difficult to determine because of the recovery without treatment or operation, as well as the absence of clinical signs involving the bony structures. The case might be regarded as one of meningitis serosa circumscripta spinalis. The high level of the lesion, unfortunately, made lumbar puncture inadvisable; hence proof or disproof of this last diagnosis is impossible. For that reason a diagnostic etiology had to be foregone.

The authors are unwilling to make a prognosis, but because of the favorable course with improvement up to date, they prefer to depend on clinical data rather than operative procedure for their guidance and opinion.

JONES, Detroit.

WEIGHT VARIABILITY OF THE NORMAL THYROID GLAND AND ITS SIGNIFICANCE. L. CASTALDI, Arch. Italiano d. Anat. e Embriol. Supplement to **18**:96, 1922.

The author has undertaken a series of anatomic researches on the endocrine glands, treating the material statistically with biometric methods. In this paper on the thyroid, the results of the statistical observation of 291 human thyroids are given. The subjects examined were aged from 2 days to 96 years. Of these 159 were male and 132 female. He found that the average weight of the thyroid is less than the figures usually given. Errors in the estimation of the thyroid weight are very likely to occur if proper consideration is not given to the age and body development of the subjects. A thyroidal index is introduced which is represented by the centesimal ratio between the stature of the individual and the cubic root of the thyroid weight. The reports of the Italian Departments of War and Agriculture on the distribution of endemic goiter in Italy are also considered.

Studying the coefficient of correlation between the weight of the thyroid and stature, the author has found that the influence of the thyroid on development, is not so great as is thought. If this influence is moderate in early age, it is minimal in the prepubertal period of greater physical development, the thyroidal index being minimal at the period of maximal growth in length (puberty). The thyroid is, therefore, more important in the phenomenon of differentiation than in the growth in length. In support of this view the author recalls the results of modern experiments with thyroidal nutrition in amphibians. There exists a very high correlation between thyroid and sexual activity, which the author examines at length. In fact, the maximal increase of its relative weight and of its absolute annual growth is found at the onset

of the sexual function, when the maximal body growth and differentiation is also found; the absolute weight reaches its maximum around the fourth and fifth decade of life, and its annual diminution begins after the menopause. The thyroid growth takes place earlier in the female in correlation with the earlier appearance of the sexual function. At birth, the absolute weight of the thyroid being equal in the two sexes, its relative weight to stature becomes larger in the female during the period of growth in height, even if the absolute weight is smaller, on account of the influence of periodical and accidental factors such as menstruation and pregnancy.

Considering the diseases suffered by the individuals studied, and their occupations, the author comes to the conclusion that diseases and system of living have no specific influence on the weight of the thyroid. Such influence is exerted instead by the orographic height, the normal thyroids in hilly districts weighing more than those of individuals living in the plains. Even the morphology of the thyroid varies according to different localities. There are variations in the frequency and length of the appendix of Morgagni, and the frequency of the accessory thyroids, which are in direct ratio to the diffusion of the strumicretinic endemy, while the absence or the incomplete development of the isthums, anomalies of defect, are in inverse ratio.

NACCARATI, New York

A CASE OF EPIDEMIC ENCEPHALITIS WITH A TREMOR TYPICAL OF MULTIPLE SCLEROSIS. G. B. HASSIN and THEODORE T. STONE, J. Nerv. & Ment. Dis. **54**:6 (Dec.) 1921.

An introductory paragraph discusses the number of types or syndromes. The case presentation is given as follows: Illness began Jan. 8, 1921, with rhinitis and a severe "sticking" pain in the hairy region of the frontal part of the head. It spread to the occiput, right arm and elbow. The pain in the head was continuous, that in the arm paroxysmal. The man kept at his work, had no cachexia or fever, and his appetite was good. Two weeks later, a tremor developed in the right arm and hand. This caused him to seek medical advice. No other changes were found in his nervous or mental condition. The tremor was especially marked on movement. Power was well preserved, but the tremor had all the ear-marks of multiple sclerosis. The left hand showed no tremor, but skilled movements were impossible with this member. Three days after the onset of the tremor and three days and two weeks after the onset of the pain, he developed diplopia, became irrational and began to sleep. He had hallucinations, sang in his sleep and talked incoherently.

Examination showed the eyes half opened, the head bent over his chest, the thighs and legs flexed and the body curved. The pupils were regular, but unequal; the left was sluggish to light, the right made no reaction. The face was mask-like. The left abdominal reflex was diminished. All other findings were negative. The patient was stuporous, lethargic and did not finish answers to questions. This condition of lethargy, pupillary abnormalities, expressionless face and extreme weakness lasted seven weeks and ended in complete recovery except for a slight right facial paresis, masklike face and a little pain in the right arm.

The discussion emphasizes the existence of tremor resembling that of multiple sclerosis rather than the types usually seen in epidemic encephalitis: myoclonic, choreiform, fascicular and fibrillary contractions.

As to pathogenesis, the authors suggest a meningeal dorsal root irritation as the cause of the pain and a ventral root meningeal irritation for the tremor. This was a meningoradicular type of encephalitis, the midbrain or polioencephalitic type following it. The authors' conclude that several types may be combined in the same clinical picture, but the preferable localization for the systemic infectious disease which we know as epidemic encephalitis is in the midbrain, regardless of the type of the disease.

CHAMBERS, Philadelphia.

GROWTH OF THE CORTICAL AND MEDULLARY SUBSTANCES OF THE ADRENAL GLANDS AND THEIR VOLUMETRIC RELATIONSHIP. L. CASTALDI, Arch. Fisiol. **20**:1 (Jan.-Feb.) 1922.

This is the second of a series of biometric studies on the endocrine glands, the first dealing with the thyroid. In this research the author used the glands of guinea-pigs instead of human adrenals, the latter being very subject to cadaveric alteration. Vast and painstaking histologic, biometric investigations were carried out on 143 suprarenal glands in 71 animals (there was one accessory gland). His calculations were obtained from drawings of many thousands of sections of the glands, with a procedure that the author describes. Reference to the works of Elliott and Tuckett, Bager, Donalson and Jackson is made.

The guinea-pig possesses adrenal glands with large relative weight to the body, and with a less relative weight of the medulla to the cortex. In embryos from 7 mm. to 32 mm. in length, the ratio of the medulla to the cortex is 1:4; at birth it becomes 1:5 and in the adult 1:9. The left adrenal gland is larger than the right, more so in postnatal than in prenatal life. The absolute weight of the glands is greater in the male, but the suprarenal index, namely the percental value of the suprarenal volume to the body weight, is also larger in the female in prenatal life. The adrenal glands of the guinea pig do not present, during prenatal development, the largest relative value to body size, such as is believed to occur in man, although complete statistical data are wanting. In pregnancy both the cortex and the medulla increase in volume. The total suprarenal index decreases, however, during the second half of pregnancy, during which the medulla shows the greatest relative diminution. In this period the fetus does not show chromaffin reaction. The coefficient of correlation between the adrenal gland and body weight is + 0.81 during the prenatal life and + 0.93 after birth. It is larger for the cortex than for the medulla. This coefficient of correlation between adrenal and body weight is much larger than the coefficient found by the same author in his study on the thyroid. This in fact, from birth to childhood, varies from + 0.64 to + 0.21.

These findings indicate that the suprarenal glands have a decided influence on body development and that such influence is exerted chiefly by the cortex. The author points out that in cerebral deformities met with in suprarenal hypoplasia, in suprarenal virilism, and in pubertas praecox from hypernephroma, it is the cortex which is increased or diminished. Experimental biology (feeding experiments) has also confirmed the important rôle that the adrenal cortex plays in the processes of body development.

In this connection the abstracter would call the attention of the reader to the recent research of another Italian investigator, L. Gazzaniga (Sperimentale **76**:121, 1922), who has found in an analysis of 83 human fetuses that the coefficient of correlation between weight of the suprarenal glands and stature is + 0.87, and between weight of the suprarenal glands and body weight is

+ 0.90. Such correspondence of results obtained in different fields is certainly conclusive for their validity; it will stimulate more investigations on the subject along the same lines.

NACCARATI, New York

TREATMENT OF THE MENINGEAL FORM OF ACUTE ENCEPHALITIS WITH ANTIMENINGOCOCCIC SERUM. W. W. HERRICK, J. A. M. A. **80**:528 (Feb. 24) 1923.

Apropos of the recent report by Helmholz and Rosenow of three cases of acute encephalitis treated with specific serum, it is of interest to record the striking effect of nonspecific serum in a case of acute encephalitis of the meningeal form. The patient was a schoolboy, aged 15, and from the symptoms of somnolence, ocular and facial palsy, myoclonia, with clear cerebrospinal fluid showing a small increase in cells and a high percentage of mononuclears, the absence of organisms on repeated smear and culture, the season and the fact of the not infrequent prevalence of the disease in the region seemed to classify this case definitely as an encephalitis.

It was apparent to observers that the effect of antimeningococcic serum in this case of acute encephalitis of the meningeal type was striking and beneficial. From the time of its administration, symptoms ceased to advance, and within thirty-six hours, the patient, who had not been expected to survive, seemed out of danger.

NIXON, San Francisco.

THE DIAGNOSIS OF EPILEPSY. HUGH T. PATRICK and DAVID M. LEVY, J. A. M. A. **79**:192 (Sept. 23) 1922.

An introductory paragraph states that the chief difficulties in the diagnosis of epilepsy are: (1) uncertainty as to what constitutes epilepsy; (2) polymorphism of the disease; and (3) lack of observation because of necessity. The conditions from which it must be differentiated are: hysteria, psychasthenia, brain tumor, syphilis, apoplexy, encephalitis, dementia praecox, melancholia, Stokes-Adams syndrome, spasmophilia, migraine, nephritis, feeblemindedness, general paralysis, multiple sclerosis, polycythemia, anemia, tic, chorea, fainting spells, infection, aural vertigo, night terror, endocrine disorder, angina pectoris, heart disease, digestive disorder, arteriosclerosis, facial spasm and laryngismus stridulus.

The authors then emphasize the very great importance of slight attacks in young persons and the frequency with which they are overlooked by the physician. They urge vigorous treatment immediately epilepsy is diagnosed, and say: "little fits do not indicate little treatment."

Proceeding then to the differentiation from hysteria and psychasthenia, cases of rather typical "epilepsy" are described, which, by hypnotism in one case and a careful history in the others, were shown to be hysterical. The authors dissent from the view that emotional conflicts, unfulfilled desires and mental maladaptation are important in the causation of epilepsy. The last case described under this heading is one of "epileptic automatism"—diagnosed by the authors as hysteria. They think that automatism lasting over one and a half hours is very rare, and is basically hysteria, provided the patient does nothing "irrational or unseemly."

Cases are given to illustrate the fact that epileptic fits may be the first sign of gross brain disease, especially when they commence between the ages of 30 and 45. They report a case of idiopathic epilepsy of jacksonian type

as an illustration of the fact that many needless operations are done on this indication. Attacks occurring without loss of consciousness are, in the authors' opinion, more frequent in children. The article is concluded by two cases thought to be psychic epilepsy, but which were shown not to be so.

CHAMBERS, Philadelphia.

THE NATURE OF CRANIAL HYPEROSTOSES OVERLYING ENDOTHELIOMA OF THE DURA. D. B. PHEMISTER, Arch. Surg. **6**:554 (March) 1923.

The importance of hyperostoses of the skull as an indication of the presence of an underlying tumor, has been emphasized in a number of recent papers. Earlier writers considered that the bony tumor was the primary growth and that the intracranial growth followed it. This theory has been disproved by more recent studies, and although the same type of tumor cell is found in both areas, the cranial hyperostosis follows the infiltration of the bone by tumor cells from the dural growth. A recent report by Cushing, based on a large number of cases of this type, shows that endotheliomatous tumors of the frontal and parietal regions, particularly those whose origin was near the falx, most frequently produce bony thickening. Particularly prone to produce an hyperostosis were the broad flat tumors spreading out over the dura and not penetrating into or markedly indenting the underlying brain. On the other hand, the tumor extending into the brain substance to a marked degree with a relatively small attachment to the dura, produced a correspondingly small amount of bony infiltration and thickening. But that the degree of overlying hyperostosis was not related definitely to the extent of the dural attachment of the tumor, was shown by cases in which rounded tumors with small dural attachment caused marked bony thickening. In every case of bony thickening, endotheliomatous invasion of the thickened bone was noted whenever the bone was examined microscopically.

Phemister reports two cases of endothelioma involving the dura and causing a thickening of the overlying bone. From the point of view of the neurologist, in one case the clinical signs were typically those of brain tumor and the exostosis was not a prominent feature; in the second case, the hyperostosis was the striking factor and nervous symptoms were entirely lacking. This latter type of case has often been diagnosed sarcoma of the skull and the underlying tumor was not suspected. He believes with Cushing that these meningeal tumors all possess sufficiently peculiar common characteristics, such as failure to make metastases, to justify separate grouping and designation as meningotheliomas or meningeomas. From a study of the cases in this report, the conclusion is reached that the hyperostosis, which develops over a considerable number of these tumors, results from the penetration of the dura and direct invasion of the skull by the tumor. The skull is penetrated by the tumor, the inner and outer tables are slightly rarified, and new bone formation from both the inner and outer tables is stimulated. The cancellous spaces of the hyperostosis are found filled, in varying degree, with tumor cells. The new bone is not tumorous in nature, but is ossified stroma of the invading endothelioma. Its spongy and radiating nature is similar to that which is seen in ossification occurring in other types of tumor, whether primary or secondary in bone and whether the new bone itself is of tumorous or nontumorous nature.

GRANT, Philadelphia.

EFFECTS OF ABLATIONS OF THE CEREBELLAR CORTEX AFTER SUPPRESSION OF THE CIRCULATION. G. Rossi, Arch. Fisiol. **20**:2 (March-April) 1922.

The author refers to his previous work on cortical cerebellar localizations (Arch. Fisiol. **19**:391, 1921), in which he studied the tonic asymmetries that follow circumscribed unilateral lesions of the cerebellar cortex, and to the work of Simonelli on a similar subject. In this article he reports the results of experiments on cadaveric rigidity in relation to postural tonus. The experiments, which were carried out in dogs and cats, are divided in three groups. In the first group are the animals in which no lesions of the nervous centers were found before the animal was killed; in the second group are those which had been deprived during life of a portion of the cerebellar cortex; in the third group are the animals in which ablation of the cerebellar cortex was performed after suppression of the circulation. The lesions of the cerebellar cortex were unilateral and involved the laminae only in their superficial portions. These ablations produce, in living animals, tonic asymmetries but no dysmetria in walking, nor the "military salute" of van Rynberk, when involving the crus primum, provided that the lesion remains superficial.

All possibility of lesion of the nuclei, in the experiments after total extraction of the blood from the animal, is excluded. The external temperature did not influence the experiments, as they were carried out in the different seasons.

The author points out that the functional territory of the cortex of the crus primum is not limited to the anterior limbs. His general conclusions are: The asymmetries produced by unilateral ablation of the cerebellar cortex are preserved, although diminished, after the death of the animal. With the advent of cadaveric rigidity, they increase in intensity. Asymmetries are also observed when the ablation of the cortex is performed several minutes after complete interruption of the circulation in the animal; they do not differ quantitatively from those which follow the ablation of the same portion of the cortex in the living animal.

This fact together with others taken in consideration in this report, demonstrates with certainty the existence of cortical cerebellar localizations absolutely independent of any primary and circulatory lesion of the cerebellar nuclei. It seems that the study of the cadaveric position of animals which during life were subjected to cerebellar lesions, represents a useful complement to the analysis of the tonic alterations produced by such lesions.

Naccarati, New York

STUDIES IN FAMILIAL NEUROSYPHILIS. II. FAMILIAL NEUROSYPHILIS FROM VARIOUS EXTRA FAMILIAL SOURCES. A CLINICAL CONTRIBUTION TO THE QUESTION OF NEUROTROPISM. J. E. Moore and A. Keidel, J. A. M. A. **80**:818 (March 24) 1923.

In three families, of which two contained three members each, and one two members, who all acquired syphilis from different sources and at different dates, all developed neurosyphilis. This occurrence can best be explained on the basis of familial predisposition. The clinical and experimental evidence now available does not settle the question as to the existence of a neurotropic strain of Spirochaeta pallida. That a neurotropic strain of organism cannot be the only factor, or necessarily the most important one, in the origin of

neurosyphilis is illustrated by the families reported in this paper, since several members, each acquiring syphilis from a separate source, all developed neurosyphilis.

NIXON, San Francisco.

THE ABDOMINAL CRISES OF MIGRAINE. J. ARTHUR BUCHANAN, J. Nerv. & Ment. Dis. **54**:5 (Nov.) 1921.

The author states: "Attacks of abdominal pain as a radical of manifestations of the migraine characteristic are exceedingly rare." However, seven case histories are given, some with tables of heredity through two and four generations. A brief summary of the important literature then follows: Under comment the author states that general physical and neurologic examination —including: eye, ear, nose and throat examination; roentgen-ray examinations of chest, kidneys, ureters, bladder, stomach and colon; blood count; urine and gastric analyses; Wassermann and cystoscopic examinations—were all negative. The most significant fact found was the association of migraine characteristics with the abdominal pain, and he emphasizes the importance of studying the family tree.

He then states that this type of abdominal pain is transmitted as a single mendelian character and therefore "becomes a biologic part of the individual of the new generation," according to the rules of heredity. "In the case of migraine, the presence of pain makes one hesitate to consider the characteristics as special types of normality. The close adherence of the transmission of migraine to the laws of heredity overcomes this doubt, and it is then a normal type."

The author concludes that a small percentage of people, "inherit and transmit at certain intervals painful and associated somatic disturbances." Pain is usually in the head but may be in the abdomen. We call this "migraine." The characteristic is unaltered by surgical or medical therapy."

CHAMBERS, Philadelphia.

RADIOGRAPHIC DIAGNOSIS OF THE SITE AND NATURE OF A VARIETY OF CEREBRAL TUMOR (PSAMMOMIAN OR ANGIOLITHIC SARCOMA). A. SOUQUES, Rev. neurol. **28**:984 (Sept.-Oct.) 1921.

The author admits that roentgen-ray examination furnishes little exact information on the site of cerebral tumors. When there are bony changes due to pressure on the cranium itself, we may get exact evidence, but this is infrequent. Changes even in the sella are of doubtful and uncertain value. Outside the forms of tumors with bony changes, it is very difficult to localize brain tumors on the basis of clinical symptoms, either because the neoplasm is in a so-called silent area, or because it has developed quite slowly and thus allows the whole brain substance to gradually adapt itself to pressure. Sometimes all we can speak of is a general intracranial pressure. It is regrettable, for this reason, that the roentgen-ray examination is too often neglected and thus surgical relief is not obtained.

According to the writer there is one particular variety of cerebral tumor that is particularly and easily localizable almost to a mathematical nicety, namely, the type referred to in the title of the paper. By way of illustration, he cites the case of Madame N., 43 years of age, whose symptoms began in May 1914, ushered in by a jacksonian seizure. The attack began with a daggerlike pain in the left hand, spread upward, involved the left forearm, arm

and face and was followed by convulsions of those parts. These attacks occurred two or three times a month, sometimes extending to the left lower extremity, with or without transitory postepileptoid hemiparesis and with or without loss of consciousness. This condition progressed for three or four years, when headache developed, then nausea and vomiting and finally impairment of vision. Postedematous optic atrophy was revealed by the ophthalmoscope in January, 1921, seven years after the onset of the first symptoms. Finally a radiographic study was made which revealed a clean cut shadow in the prerolandic area, close to the inter-hemispherical falx and behind and below the eyes. Operation was successful with relief of all the chief symptoms. A tumor about the size of a large mandarin was removed. It was clearly a psammomian or angiolithic sarcoma.

The conclusions are: (1) a radiographic study should be made in every case where there is even the suspicion of a cerebral tumor; (2) in angiolithic tumors, the radiograph not only reveals the site of the growth, but reveals its form, volume, and relations to neighboring structures; (3) it enables us immediately to recognize its psammomatous nature; (4) it serves as a guide for surgical operation; (5) these facts are all the more important as the psammomian bodies are benign, removable, and their removal results in radical cure.

JONES, Detroit.

INTERNAL HEMORRHAGIC PACHYMENINGITIS IN INFANCY: C. W. BURHANS and H. J. GERSTENBERGER, J. A. M. A. **80**:604 (March 3) 1923.

Numerous theories as to the etiology of internal hemorrhagic pachymeningitis have been advanced. The authors state that perhaps the most plausible theory at present is that of Rosenberg, who believes that this disease is due to thrombosis of the cavernous sinus, as the result either of an infection or of a marantic condition. In the cases reported in this paper, trauma at birth or later, or both, seems to have been the most important etiologic factor.

Vomiting and convulsions are perhaps the most common reasons for bringing the patient to the physician. Puncture of the anterior fontanel outside the longitudinal sinus is a procedure on which pediatricians have laid much stress. To obtain by it a yellow or bloody fluid practically makes the diagnosis certain. This fluid—and the same is true when it is obtained from the lumbar subarachnoid space—does not clot on standing, although there may be a small fibrin clot or pellicle. Briefly, then, if an infant more than 4 weeks old, usually between the ages of 6 and 18 months, has symptoms of markedly increased intracranial pressure, often more acute than with a tumor, and has a normal spinal fluid, one of the first things to consider is internal hemorrhagic pachymeningitis. The presence of retinal hemorrhages makes the diagnosis practically certain, and a positive fontanel puncture is pathognomonic. A yellow subarachnoid fluid or one containing red blood cells is very suggestive. If the disease has been going on for some time, there will probably be enlargement of the head.

NIXON, San Francisco.

CONTRIBUTION TO THE KNOWLEDGE OF PALILALIA. T. SENISE, Cervello **1**:4 (July-Aug.) 1922.

Two cases presenting the phenomenon of palilalia are described in this paper. Palilalia is a rare disturbance of the central mechanism of speech consisting in the spontaneous and involuntary repetition by the patient, for

several consecutive times (cases have been registered up to twenty-one times), of his own words. Reported by Brissaud previous to 1899, it was well described by Souques in 1908, and subsequently by a few other authors. This phenomenon has been observed in different serious organic diseases of the brain, particularly in pseudobulbar paralysis, but also in senile dementia, in general paralysis, in cerebral tumors and in the parkinsonian syndromes from epidemic encephalitis. In almost all the cases reported, a more or less conspicuous degree of mental enfeeblement, and very frequently also a certain amount of sensory aphasia and verbal amnesia, not rarely also a slight dysarthria, were noticed. The cases reported by Souques and by Trénel and Crinon are the only two on record in which a necropsy was made. In both, lesion of the corpus callosum was found. In one of the two cases here reported by Senise, no lesion of the callosum was found. The patient, a man aged 72, intra vitam had suffered from senile dementia and, besides palilalia, showed word deafness and paralexia. The necropsy revealed: softening of the cerebral cortex, especially in the right lobulus paracentralis and in the left superior parietal convolution; marked atrophy of the whole left temporal lobe; and extensive focal destruction of the white substance in the left occipital lobe. In discussing the genetic mechanism of the phenomenon of palilalia the author rejects the views of P. Marie and Lévy who admit a particular specific lesion for its production. He considers this a phenomenon of *excess*, which, while it is independent of the functional integrity of the phasicomotor and verbomotor center, is conditioned by the most diverse lesions of the centers and pathways connected with this center. He concludes, therefore, stating that palilalia should be interpreted as a *functional phenomenon of release* of the Broca center (intact) from the other centers that, in normal conditions, regulate and dominate it (the most important being Wernicke's center, where a frequent coexistence of palilalia with lesions of the left temporal lobe is seen). It is therefore essentially a spasmodic phenomenon of the expressive center of speech, *a kind of clonus of the motor center of speech.*

NACCARATI, New York.

THE SACHS-GEORGI REACTION IN NEUROSYPHILIS. S. A. LEVINSON and W. F. PETERSEN, J. Nerv. & Ment. Dis. **54**:5 (Nov.) 1921.

The authors, in a comparative study of the Wassermann reaction and Sachs-Georgi reaction for syphilis, recently published, found the Sachs-Georgi reaction positive in every case where the Wassermann reaction was positive, but also positive in many where the Wassermann reaction was negative. These were mostly cases of clinical neurosyphilis. They state that "the Wassermann test has not been as successful in aiding our diagnosis of early syphilis of the nervous system as we might wish" and they emphasize the great importance of its early recognition. The adoption of the Sachs-Georgi reaction in diseases of the central nervous system would seem desirable because of its simple technic, its earlier appearance, its longer positive findings and the fact that it is frequently positive in congenital, latent and parasyphilitic disease.

In the summary it is stated that in an examination of the serum or spinal fluid of 100 cases of neurosyphilis (tabes, general paralysis, cerebrospinal syphilis etc., an agreement of 78 per cent. was found between the Wassermann and the Sachs-Georgi reactions. The Sachs-Georgi reaction was positive in eighteen cases where the Wassermann reaction was negative. They

conclude that the simplicity of the Sachs-Georgi reaction renders it a valuable aid in the diagnosis of neurosyphilis, used alone, as a control of the Wassermann reaction or supplementing it.

CHAMBERS, Philadelphia.

PERIARTERIAL SYMPATHECTOMY. ALBERT E. HALSTEAD and FREDERICK CHRISTOPHER, J. A. M. A. **80**:173 (Jan. 20) 1923.

Periarterial sympathectomy was performed by the authors to relieve pain in the foot, the result of an endarteritis obliterans. The femoral artery of the right leg was dissected out so that the junction of the middle and lower thirds was visible and the adventitia was incised and stripped completely off for a distance of 5 cm. The patient's work requires him to be on his feet about twelve hours daily and he is able to walk a mile or more. There is no pain in the leg except a slight one if he walks rapidly. Numbness, which was present at the time of operation, has practically disappeared. Before the operation, the patient was unable to do anything, and the pain was most severe when lying in bed. Now there is no pain. The general health is excellent. The leg used to be cold but gets warm in bed now. Tactile and thermal discriminations are normal.

NIXON, San Francisco.

OSTEOMA OF THE SKULL. C. W. RAND, Arch. Surg. **6**:573 (March) 1923.

Two cases of osteoma of the skull, one being associated with a large underlying endothelioma, are reported. In the first case, a large section of the calvarium had been removed some time before, the operator believing that he was dealing simply with a benign osteoma of the skull. At this time it was noted that there were several spicules of bone growing down through the dura and that the cortex was covered with abnormal tissue. The dura at this point was apparently destroyed. Four years later, another area of cranial thickening had formed toward the midline from the point of the previous operation and there was evidence of new bone formation in the cranial defect caused by the previous operation. A ventriculogram showed that the left ventricle was occluded and the right anterior horn pushed down by the tumor mass. A large endothelioma was removed from the midline that involved the longitudinal sinus and both anterior lobes, especially the left. The patient made an uneventful recovery and is reported as clinically much improved. Pathologic examination revealed that the tumor was an endothelioma of the meninges.

The sequence of events in this case is interesting. The tumor showed a marked tendency to penetrate the bone and even stimulated the osteogenetic power of the dura sufficiently to form new bone in the defect caused by the first operation. This seems to uphold the theory that one effect of these meningeomas is actually to stimulate new bone growth, as well as to cause bony thickening by the penetration of the bone by tumor cells.

The second case was that of a simple osteoma of the skull not associated with any true intracranial growth. It was successfully removed at operation with amelioration of symptoms.

GRANT, Philadelphia.

MAGNESIUM SULPHATE AS A SEDATIVE. P. G. WESTON AND M. Q. HOWARD, Am. J. Med. Sc. **165**:431 (March) 1923.

The authors obtained a pure form of the magnesium salt by recrystallization, which was then made into a 50 per cent. solution and sterilized. When used in doses of 2 c.c. subcutaneously, it was never found to give pain or to be

followed by sloughing. In their series of over one thousand cases the effects were striking. After fifteen to thirty minutes, relief was obtained in 82 per cent. of cases and the patients became quiet and in many cases sleep was obtained. In only 6 per cent. of the cases was a second dose required to bring the required effect. The remainder, who were unaffected by the use of this method, also failed to respond to other sedatives and were only controlled with heroic doses of morphin. These patients all fell in the group of active and noisy inmates with whom sedation of any kind was difficult. The authors consider it an efficient method of controlling marked excitement in certain forms of insanity and its use in other fields is advocated.

TEMPLE FAY, Philadelphia

THREE CASES OF ACUTE ENCEPHALITIS TREATED WITH SPECIFIC SERUM. HENRY F. HELMHOLZ and EDWARD C. ROSENOW, J. A. M. A. **79**:2068 (Dec. 16) 1922.

This serum was obtained from a horse repeatedly injected with a streptococcus isolated from a patient suffering from typical encephalitis. Three cases are reported and they thought it advisable to report this small group, with the hope of interesting others in the specific treatment of encephalitis, in order to determine whether the same excellent results can be obtained in a larger series of cases. With the injection of the serum there was a decided improvement in the patients' general condition and a complete clearing up of the nervous symptoms of encephalitis. They have also shown that the serum protects animals against disease following intracerebral injections of the streptococcus, which is not the case with normal horse serum.

NIXON, San Francisco.

Book Reviews

EINFUEHRUNG IN DIE KLINIK DER INNEREN SEKRETION. By Prof. G. Peritz, M.D., Nervenarzt in Berlin. Paper. Price 27 marks. Pp. 257 with 31 illustrations. Berlin: S. Karger, 1923.

So much both good and bad has been written in recent years on the subject of the endocrine glands that it is difficult for the student to secure a clear view of what has actually been established. In this book, Peritz has collected together, in admirably concise form, what may be considered as the fundamental facts. He has contented himself largely with stating these facts, but has indicated sufficiently the general trend of opinion and the possibilities for future development. Each gland is considered separately and a brief summary is given of the anatomy and histology. Function is illustrated by clinical data as well as by the experimental evidence available. A chapter is then devoted to the pluriglandular syndromes which are treated conservatively and with frank admissions of lack of knowledge. The known facts of chemistry of the secretions are reviewed briefly and clearly.

The reciprocal relations between the endocrine and the nervous systems are discussed at some length, with diagrammatic representations of the nervous connections from various sources. The methods of functional investigation, both physical and pharmaceutical are given in a clear and practical manner. Finally a chapter is devoted to the relation of the endocrines to the "constitution" by which is meant the mode of reaction of the organism to the environment, both structurally and functionally. Under this head are discussed hyperthyroidism, infantilism, status thymicolymphaticus, susceptibility to tuberculosis, spasmophilia, schizophrenia, etc.

The book is strictly a compilation and is not offered as an original contribution. It is intended as a text book for students and practitioners, to serve as a foundation for practice or further investigation. In the text the author mentions the names of many investigators but has intentionally refrained from giving bibliographic references for the reason that their inclusion would make the book altogether too large. The selection of a few references to the more important contributions would be a task of some difficulty, but would serve to make the book more valuable by providing points of access to the literature. There is a fairly good index. The material is well arranged, the descriptions are simple, the illustrations are well chosen, and the book can be recommended without hesitation to the student and practicing physician.

DER SELBSTMORD. By Privatdozent Dr. med. R. Weichbrodt. Abhandlungen aus der Neurologie, Psychiatrie, Psychologie und Ihren Grenzgebieten. Beiheft 22 zur Monatsschrift für Psychiatrie und Neurologie herausgegeben von K. Bonhoeffer. Paper. Pp. 44. Berlin: S. Karger, 1923.

In this brief monograph the author has collected a series of statistics of suicide and discusses the factors that enter into its etiology. He points out that suicide has been known from the most ancient times, though it has unquestionably increased greatly within recent years. There is no name for suicide used in the Bible and but four examples are given in this history which covers many thousand years. Suicide has increased greatly in almost

all European countries in the past fifty years, but has been almost stationary in Denmark and Ireland and has actually diminished in one country—Norway. One striking fact that is brought out relates to the enormous increase that has occurred among the Jews in Germany as compared with people of other creeds. To illustrate this the following figures, which represent the rates per million living, may be quoted:

	Catholics	Protestants	Jews
1849-1855.....	50	160	46
1901-1907.....	101	252	294

A notable increase is also observable in the number of women who commit suicide. The rate among men has increased in thirteen years by 20 per cent.; that for women by 70 per cent. Whereas, in 1893, the proportion of men to women suicides was about 4:1, it has since become less than 3:1.

Weichbrodt discusses, with frequent references to ancient and modern literature, the relations of suicide to mental abnormality, sex, age, season of year, etc., in which there is little new brought out. He reaches the conclusion that the most important factor in the causation of suicide is the struggle for existence. This is indicated by the increasing rate in women, who are gradually assuming more and more of the burdens that used to be left to men. Suicide is uncommon among the very poor, but frequent in those who have known better times. The second factor of importance is the attitude toward life that is expressed by religious observance. It is not a question of particular creeds, but of the devotion to an ideal, which seems to act as a balance wheel in meeting difficulties.

This little book is well worth reading and contains many figures that will be found useful. The views expressed and conclusions reached are of considerable importance to those interested in social psychology and psychiatry in its broader aspects.